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# Palladium-Catalyzed Tandem Reaction to Construct Benzo[c]phenanthridine: Application to the Total Synthesis of Benzo[c]phenanthridine alkaloids

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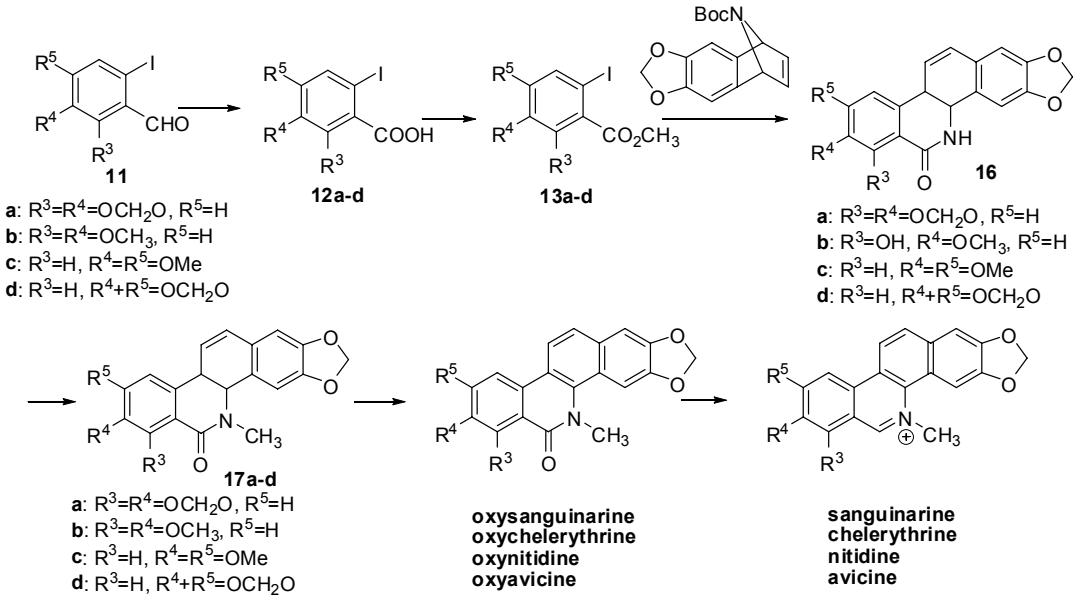
**Part 1. Experimental Procedures and Analytical Data**

**General Methods:** All reactions were carried out under an argon atmosphere, and all commercially available reagents were used without further purification. Tetrahydrofuran and toluene were purified by distillation under $N_2$ from Na/benzophenone immediately prior to use. NMR spectra were recorded with a spectrometer using $CDCl_3$ or dmso-$d_6$. Chemical shifts (δ) were reported in partsper million (ppm) relative to either a tetramethylsilane internal standard or solvent signals. The melting points were determined and uncorrected. Compounds **9**[1] were synthesized according to literature procedures. The suitably functionalized 2-iodobenzaldehyde **11c**, **11d** were synthesized according to literature[2], **11a** and **11b** were prepared according to the methods to the litetature.[3, 4, 5]




**General Procedure for the substituted benzoic acids 12a-d:** To a stirred solution of 50% aq. KOH (3.5 mL, 48 mmol) and *o*-iodo benzaldehyde (12 mmol) in methanol (20 mL) at 65 $^oC$, aqueous

hydrogen peroxide (30%, 9.6 mL, 96 mmol) was added dropwise during 20 min, The mixture was then stirred at the same temperature for 10 min, cooled, acidified with concentrated hydrochloride and flitrated to give benzoic acid.

5-**iodobenzo[d][1,3]dioxole-4-carboxylic acid 12a:** This compound was obtained in 98% yield; mp: 198-201 $^{o}$C. IR (KBr): ν =1692 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, dmso-$d_6$) δ: 13.61 (s, 1H), 7.35 (d, $J$ =8 Hz, 1H), 7.81 (d, $J$ =8 Hz, 1H), 6.12 (s, 2H). $^{13}$C NMR (100 MHz, dmso-$d_6$) δ: 165.9, 148.0, 145.8, 132.2, 121.1, 111.5, 102.2, 81.6. HRMS (ESI): calcd for $[C_8H_5IO_4\text{-}H]^-$: 290.9160; found: 290.9163.

**6-iodo-2,3-dimethoxybenzoic acid** 12**b:** This compound was obtained in 97% yield; mp: 128-131 $^{o}$C (lit.[6] 137-138 $^{o}$C). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, $J$ =8.4 Hz, 1H), 6.74 (d, $J$ =8.4 Hz, 1H), 3.92 (s, 3H), 3.88 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 171.5, 153.0, 146.9, 134.7, 134.1, 115.6, 79.1, 61.9, 56.1. HRMS (ESI): calcd for $[C_9H_9IO_4\text{-}H]^-$: 306.9473; found: 306.9480.

**2-iodo-4,5-dimethoxybenzoic acid 12c:** This compound was obtained in 97% yield; mp: 197-200 $^{o}$C (lit.[7] 159-160 $^{o}$C). $^{1}$H NMR (400 MHz, dmso-$d_6$) δ: 13.06 (s, 1H), 7.43 (s, 1H), 7.38(s, 1H), 3.83 (s, 3H), 3.78 (s, 3H); $^{13}$C NMR (100 MHz, dmso-$d_6$) δ: 166.9, 151.3, 148.2, 127.1, 123.1, 113.5, 84.7, 55.9, 55.5. HRMS (ESI): calcd for $[C_9H_9IO_4\text{-}H]^-$: 306.9473; found: 306.9472.

**6-iodobenzo[d][1,3]dioxole-5-carboxylic acid 12d:** This compound was obtained in 98% yield; mp: 221-223 $^{o}$C (lit.[8] 216-217 $^{o}$C). $^{1}$H NMR (400 MHz, dmso-$d_6$) δ: 13.1 (s, 1H), 7.51 (s, 1H), 7.32 (s, 1H), 6.14 (s, 2H). $^{13}$C NMR (100 MHz, dmso-$d_6$) 167.0, 150.4, 147.7, 129.0, 119.8, 110.1, 102.5, 85.0. HRMS (ESI): cacld. for $[C_8H_5IO_4\text{-}H]^-$: 290.9160; found: 290.9156.

**General Procedure for the functionalized methyl *o*-iodobenzoate 13a-d:** To a stirred solution of benzoic acid (0.01 mol) in $CH_2Cl_2$ (50 mL), oxalyl chloride (5.08 g, 0.02 mol) was added, then drops of DMF was added to catalyzed the forming of benzoyl chloride. After all the benzoic acid dissolved, the mixture was stirred 2 h, then the solvent and excess oxalyl chloride removed under reduce pressure and 30 mL of methanol was added to the residue. After the solution was stirred 30 min, 70 mL $CH_2Cl_2$ was added, washed with water and dried over $MgSO_4$, filtered, and concentrated. The residue was purified

by column chromatographic on silica gel with petroleum ether/ethyl acetate in the ratio to afford the methyl *o*-iodobenzoate.

**Methyl 5-iodobenzo[d][1,3]dioxole-4-carboxylate 13a:** 8% ethyl acetate/petroleum ether; white solid (2.99g, 98%); mp: 51-54 $^{o}$C. IR (KBr): ν =1708 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, *J* =8 Hz, 1H), 6.63 (d, *J* =8 Hz, 1H), 6.06 ( s, 2H), 3.96 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 165.0, 148.6, 147.4, 133.3, 119.1, 112.0, 102.3, 81.5, 52.6. HRMS (ESI): cacld. for $[C_9H_7IO_4+Na]^+$: 328.9281; found: 328.9282.

**methyl 6-iodo-2,3-dimethoxybenzoate 13b:** 10% ethyl acetate/petroleum ether; white solid (3.2g, 97%); mp: 57-60 $^{o}$C (lit.[6] 57-59 $^{o}$C). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, *J* =8.8 Hz, 1H), 6.71 (d, *J* =8.8 Hz, 1H), 3.96 (s, 3H), 3.85 (s, 3H), 3.85 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 167.5，153.0，146.8 ， 135.5， 134.3， 115.2， 79.4， 61.8, 56.0， 52.8. HRMS (ESI): cacld. for $[C_{10}H_{11}IO_4+Na]^+$: 344.9594; found: 344.9598.

**Methyl 2-iodo-4,5-dimethoxybenzoate 13c:** 10% ethyl acetate/petroleum ether; white solid (3.2 g, 97%); mp: 104-107 $^{o}$C (lit.[9] 105-107 $^{o}$C). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.45 (s, 1H), 7.40 (s, 1H), 3.92 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 165.9, 151.9, 148.6, 126.0, 123.7, 113.8, 84.7, 56.3, 56.0, 52.3. HRMS (ESI): cacld. for $[C_{10}H_{11}IO_4+H]^+$: 322.9775; found: 322.9775.

**Methyl 6-iodobenzo[d][1,3]dioxole-5-carboxylate 13d:** 8% ethyl acetate/petroleum ether; white solid (2.99 g, 98%); mp: 78-80 $^{o}$C (lit.[10] 84.6-86.1 $^{o}$C). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.41 (s, 1H), 7.37 (s, 1H), 6.05 (s, 2H), 3.89 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 165.9, 151.1, 148.1, 127.5, 120.9, 111.0, 102.4, 84.9, 52.4. HRMS (ESI): cacld. for $[C_9H_7IO_4+Na]^+$: 328.9281; found: 328.9286.

**General Procedure cyclization of *o*-iodo benzoate with azabicyclic alkene**: To a solution of azabicycle **9** (1.20 mmol, 0.344 g), Methyl *o*-iodo-benzoate (1.00 mmol) and THF (20 mL) were added $Pd(PPh_3)_2Cl_2$(0.02 mmol, 14 mg), zinc powder (10 mmol, 0.654 g), and zinc chloride (0.5 mmol, 68 mg). The mixture was heated at 60 $^{o}$C under $N_2$ atmosphere. After Methyl *o*-iodo-benzoate disappeared

(monitored by TLC), the reaction mixture was cooled, diluted with methylene chloride (15 mL). Then it was filtered through a short pad of Celite silica gel and washed with $CH_2Cl_2$ several times. After concentration in vacuo, the crude product was purified by silica gel column using ethyl acetate/ petroleum ether as the eluent to give the corresponding *cis*-dihydro benzo[c]phenanthridinone.

***cis*-dihydro benzo[c]phenanthridrinone 10:** 50% ethyl acetate/petroleum ether; off-white solid (262 mg, 90%); mp: decomposed at 260 $^oC$. IR (KBr): ν =1665 $cm^{-1}$ (C=O). $^1H$ NMR (400 MHz, $CDCl_3$ ) δ: 8.08 (d, *J* =7.2 Hz, 1H), 7.53 (m, 1H), 7.40(m, 1H), 7.31 (d, *J* =7.2 Hz, 1H), 6.78 (s, 1H), 6.67 (s, 1H), 6.45 (t, *J* =2.8 Hz , 1H), 5.98 (d, *J* =1.6 Hz, 2H), 5.69 (t, *J* =2.4 Hz , 1H), 5.59 (s, 1H), 4.77 (d, *J* =5.6 Hz, 1H), 3.84(dd, *J* =2.8 Hz, 2.4 Hz, 1H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 165.1, 148.1, 147.3, 139.7, 133.0, 128.0, 127.7, 127.3, 127.1, 127.0, 126.9, 125.7, 108.4, 107.8, 101.4, 52.5, 38.8.. HRMS (ESI): calcd for $[C_{18}H_{13}NO_3+Na]^+$: 314.0787; found: 314.0781.

***cis*-dihydro benzo[c]phenanthridinone 16a:** 66% ethyl acetate/petroleum ether; off-white solid (305 mg, 91%); mp: decomposed at 260 $^oC$. IR (KBr): ν =1668 $cm^{-1}$ (C=O). $^1H$ NMR (400 MHz, $CDCl_3$ ) δ: 6.92 (d, *J* =7.6 Hz, 1H), 6.77 (s, 1H), 6.75 (d, *J* =8 Hz, 1H), 6.66 (s, 1H), 6.43 (d, *J* =9.2 Hz, 1H), 6.13 (d, *J*=8.4 Hz, 2H), 5.98 (s, 2H), 5.68 (d, *J* =8.4 Hz, 1H), 5.54 (s, 1H), 4.69 (d, *J* =9.2 Hz, 1H), 3.75(s, 1H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ:163.1, 148.3, 148.0, 147.8, 147.2, 133.0, 127.4, 127.3, 127.0, 125.7, 119.6, 111.8, 108.3, 107.7, 102.5, 101.4, 52.8, 38.6. HRMS (ESI): calcd for $[C_{19}H_{13}NO_5+Na]^+$: 358.0686; found: 358.0689.

***cis*-dihydro benzo[c]phenanthridinone 16b:** 70% ethyl acetate/petroleum ether; off-white solid (273 mg, 81%); mp: decomposed at 270 $^oC$. IR (KBr): ν =1659 $cm^{-1}$ (C=O). $^1H$ NMR (400 MHz, $CDCl_3$ ) δ: 12.37 (s, 1H), 6.99 (d, *J* =7.6 Hz, 1H), 6.76 (s, 1H), 6.70 (s, 1H), 6.67 (s, 1H), 6.68 (d, *J* =8.4 Hz, 1H), 6.42 (d, *J* =8.8 Hz, 1H), 5.99 (s, 2H), 5.73 (s, 1H), 5.60 (d, *J* =8.4 Hz, 1H), 4.73 (s, 1H), 3.89 (s, 3H), 3.76(s, 1H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 169.6, 151.9, 148.3, 147.6, 147.3, 131.3, 127.7, 127.4, 126.7, 124.8, 116.5, 116.3, 110.1, 108.5, 107.8, 101.5, 56.2, 53.0, 38.3. HRMS (ESI): calcd for $[C_{19}H_{15}NO_5+Na]^+$: 360.0842; found: 360.0847.

***cis*-dihydro benzo[c]phenanthridinone 16c:** 66% ethyl acetate/petroleum ether; off-white solid (316 mg, 90%); mp: decomposed at 270 $^{o}$C. IR (KBr): ν =1662 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$ ) δ: 7.58 (s, 1H), 6.79 (s, 1H), 6.76 (s, 1H), 6.68 (s, 1H), 6.46 (d, *J* =8 Hz, 1H), 5.99 (s, 2H), 5.69 (d, *J* =8.0 Hz, 1H), 5.56 (s, 1H), 4.76 (s, 1H), 3.96 (s, 3H), 3.95 (s, 3H), 3.77 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 165.3, 153.0, 148.4, 148.0, 147.3, 133.3, 127.3, 127.0, 126.7, 125.9, 120.5, 110.0, 109.2, 108.4, 107.7, 101.4, 56.2, 52.7, 38.4. HRMS (ESI): calcd for $[C_{20}H_{17}NO_5+Na]^+$: 374.0999; found: 374.0996.

***cis*-dihydro benzo[c]phenanthridinone 16d:** 66% ethyl acetate/petroleum ether; off-white solid (295 mg, 88%); mp: decomposed at 270 $^{o}$C. IR (KBr): ν =1663 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$ ) δ: 7.52 (s, 1H), 6.75 (s, 1H), 6.67 (s, 1H), 6.46 (s, 1H), 6.46 (d, *J* =9.2 Hz, 1H), 6.03 (d, *J* =5.6 Hz, 2H), 5.99 (s, 2H), 5.68 (d, *J* =9.2 Hz, 1H), 5.65 (s, 1H), 4.73 (s, 1H), 3.75 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 164.8, 151.5, 148.0, 147.3, 147.3, 135.2, 127.3, 127.1, 126.5, 125.9, 122.1, 108.4, 107.8, 107.7, 106.9, 101.7, 101.4, 52.5, 38.7. HRMS (ESI): calcd for $[C_{19}H_{13}NO_5+Na]^+$: 358.0686; found: 358.0688.

**General Procedure for *N*-methyl *cis*-dihydro benzo[c]phenanthridinone:** A mixture of *cis*-dihydron benzo[c]phenanthidinone **16a-d** (0.6 mmol), KOH (1.8 mmol, 100 mg), $CH_3I$ (1.2 mmol, 170 mmg) and $CH_3COCH_3$ (15 mL) was stirred and warmed to reflux for about 2 h with TLC monitoring. Then 70 mL $CHCl_3$ was added, washed with water and brine, and dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatographic on silica gel with petroleum ether/ethyl acetate to afford the *N*-methyl *cis*-dihydro benzo[c]phenanthridinone.

***N*-methyl *cis*-dihydro benzo[c]phenanthridinone 17a:** 50% ethyl acetate/petroleum ether; off-white solid (209 mg, 100%); mp: decomposed at 270 $^{o}$C. IR (KBr): ν =1651 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, dmso-$d_6$) δ: 8.29 (s, 1H), 7.70 (s, 1H), 7.69 (d, *J* =8 Hz, 1H), 7.31 (s, 1H), 7.29 (s, 1H), 7.28 (s, 1H), 7.03 (d, *J* =8 Hz, 1H), 6.94 (d, *J* =8 Hz, 1H), 6.13 (s, 2H), 6.10 (s, 2H), 2.57 (s, 3H). $^{13}$C NMR (100 MHz, dmso-$d_6$) δ: 164.9, 147.5, 147.3, 146.4, 144.8, 135.8, 133.0, 130.0, 128.9, 126.5, 125.9, 124.8, 123.0, 119.5, 108.6, 103.6, 103.2, 101.5, 101.2, 25.8. HRMS (ESI): calcd for $[C_{20}H_{15}NO_5+Na]^+$: 372.0842; found: 372.0841.

***N*-methyl *cis*-dihydro benzo[c]phenanthridinone 17b:** 50% ethyl acetate/petroleum ether; off-white solid (219 mg, 100%); mp: decomposed at 280 $^{o}$C. IR (KBr): ν =1651 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$ ) δ: 6.82 (s, 2H), 6.65 (s, 1H), 6.50 (s, 2H), 6.35 (d, *J* =7.2 Hz, 1H), 5.86 (d, *J* =12.8 Hz, 1H), 4.66 (d, *J* =7.2 Hz, 1H), 3.95 (s, 3H), 3.78 (s, 3H), 3.76 (d, *J* =12.8 Hz, 1H), 3.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 162.7, 152.8, 149.1, 147.6, 146.7, 131.2, 128.9, 126.9, 125.8, 124.2, 120.6, 114.7, 111.0, 107.3, 105.8, 101.1, 61.6, 61.3, 55.9, 36.1, 35.6. HRMS (ESI): calcd for $[C_{21}H_{19}NO_5+Na]^+$: 388.1155; found: 388.1150.

***N*-methyl *cis*-dihydro benzo[c]phenanthridinone 17c:** 50% ethyl acetate/petroleum ether; off-white solid (219 mg, 100%); mp: decomposed at 280 $^{o}$C. IR (KBr): ν =1663 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$ ) δ: 7.50 (s, 1H), 6.71 (s, 1H), 6.67 (s, 1H), 6.59 (s, 1H), 6.38 (d, *J* =9.6 Hz, 1H), 5.91 (s, 2H), 5.61 (d, *J* =9.6 Hz, 1H), 5.47 (s, 1H), 4.68 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.69 (s, 1H), 1.18 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 165.3, 153.0, 148.5, 148.1, 147.3, 133.3, 127.3, 127.0, 126.7, 125.8, 120.4, 110.0, 109.2, 108.4, 107.7, 101.4, 56.2, 52.7, 38.4, 29.7. HRMS (ESI): calcd for $[C_{21}H_{19}NO_5+Na]^+$: 388.1155; found: 388.1153.

***N*-methyl *cis*-dihydro benzo[c]phenanthridinone 17d:** 50% ethyl acetate/petroleum ether; off-white solid (209mg, 100%); mp: decomposed at 280 $^{o}$C. IR (KBr): ν =1647 cm$^{-1}$ (C=O). $^{1}$H NMR (400 MHz, $CDCl_3$ ) δ: 7.45 (s, 1H), 6.60 (br s, 2H), 6.54 (br s, 2H), 6.31 (s, 1H), 5.94 (s, 2H), 5.89 (s, 2H), 4.68 (s, 1H), 3.78 (s, 1H), 3.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 163.9, 150.5, 147.6, 146.8, 133.4, 129.2, 127.1, 125.1, 125.1, 124.2, 107.8, 107.4, 105.8, 105.8, 105.6, 101.4, 61.1, 35.5, 29.7. HRMS (ESI): calcd for $[C_{20}H_{15}NO_5+Na]^+$: 372.0842; found: 372.0846.

**General Procedure for oxybenzo[c]phenanridines**: To a suspension of *N*-methyl *cis*-dihydron benzo[c]phenanthidinone **17a-d** (0.3 mmol) and DDQ (136 mg, 0.6 mmol) in benzene (10 mL) was refluxed for about 2 h with TLC monitoring. After the dihydron compound disappeared, $CHCl_3$ (80 mL) was added, the mixture was successively washed with $H_2O$ (15 mL), 1 N NaOH (10 mL×3), $H_2O$ (15 mL), and brine (15 mL), dried ($Na_2SO_4$), and evaporated. The residue was purified by column

chromatography on silica gel with ethyl acetate/ petroleum ether as the eluent to give the oxybenzo[c]phenanridines.

**Oxysanguinarine**: 50% ethyl acetate/petroleum ether; off-white solid (98 mg, 94%); mp: 361-363 $^{o}$C (lit.[11] 366-368 $^{o}$C). IR (KBr): ν =1649 cm$^{-1}$ (C=O). $^{1}$HNMR: (400 MHz, CDCl3 ) δ: 7.98 (d, *J* =8.8 Hz, 1H), 7.76 (d, *J* =8.4 Hz,1H), 7.59( s, 1H), δ=7.54 (d, *J* =8.4 Hz, 1H), 7.25 (d, *J* =8.4 Hz, 1H), 7.17(s, 1H), 6.28 (s, 2H), 6.10 (s, 2H), 3.91 (s, 3H). HRMS (ESI): calcd for $[C_{20}H_{13}NO_5+Na]^+$: 370.0686; found: 370.0682.

**Oxychelerythrine**: 50% ethyl acetate/petroleum ether; off-white solid (101 mg, 93%); mp: 198-200 $^{o}$C (lit.[12] 199-201 $^{o}$C). IR (KBr): ν =1646 cm$^{-1}$ (C=O). $^{1}$H NMR: (400 MHz, $CDCl_3$ ) δ: 7.99 (s, 1H), 7.97 (s, 1H), 7.53 (s, 1H), 7.52 (d, *J* =9.2 Hz, 1H), 7.38 (d, *J* =9.2 Hz, 1H), 7.15 (s, 1H), 6.09 (s, 2H), 4.08 (s, 3H), 3.98 (s, 3H), 3.89 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 162.6, 152.6, 150.0, 147.5, 147.0, 135.6, 131.6, 128.8, 123.3, 120.9, 119.7, 118.4, 117.8, 117.7, 104.6, 102.5, 101.5, 61.8, 56.5, 40.8. HRMS (ESI): calcd for $[C_{21}H_{17}NO_5+Na]^+$: 386.0999; found: 386.0996.

**Oxynitidine**: 50% ethyl acetate/petroleum ether; off-white solid (103 mg, 95%); mp: 270-272 $^{o}$C (lit.[13] 276-278 $^{o}$C). IR (KBr): ν =1626 cm$^{-1}$ (C=O). $^{1}$H NMR: (400MHz, $CDCl_3$) δ: 7.97 (d, *J* =8.8 Hz, 1H), 7.92 (s, 1H), 7.62 (s, 1H), 7.57 (s, 1H), 7.54 (d, *J* =8.8 Hz, 12H), 7.17 (s, 1H), 6.10 (s, 2H), 4.10 (s, 3H), 4.06 (s, 3H), 3.97 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 164.3, 153.5, 149.7, 147.5, 147.0, 135.9, 131.8, 128.9, 123.2, 121.0, 119.1, 118.3, 116.6, 108.6, 104.8, 102.8, 102.6, 101.5, 56.3, 56.1, 41.2. HRMS (ESI): calcd for $[C_{21}H_{17}NO_5+Na]^+$: 386.0999; found: 386.0995.

**Oxyavicine**: 50% ethyl acetate/petroleum ether; off-white solid (97 mg, 93%); mp: 271-273 $^{o}$C (lit.[14] 276-277 $^{o}$C). IR (KBr): ν =1646 cm$^{-1}$ (C=O). $^{1}$H NMR: (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* =8.4 Hz, 1H), 7.91 (s, 1H), 7.63 (s, 1H), 7.61 (s, 1H), 7.55 (d, *J* =8.4 Hz, 1H), 7.18 (s, 1H), 6.15 (s, 2H), 6.12 (s, 2H), 3.98 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 164.1, 152.4, 148.2, 147.6, 147.0, 135.8, 131.0, 123.3, 120.9, 120.7, 118.5, 116.8, 106.6, 104.8, 102.7, 102.0, 101.6, 100.7, 41.2. HRMS (ESI): m/z(%) calcd for $[C_{20}H_{13}NO_5+Na]^+$: 370.06866; found: 370.0693.

**General Procedure for benzo[c]phenanthridinium chloride:** $LiAlH_4$ (13.6 mg, 0.6 mmol)was added to a solution of oxybenzo[c]phenanthridine (0.2 mmol) in anhyd THF (5 mL) and the mixture was stirred for 20 min at r.t., Excess hydride was decomposed with wet $Et_2O$, and the organic layer was concentrated. The residue was treated with 10% HCl (5 mL) at r.t., the resulting precipitates were collected by filtration to produce desired quaternary base salt.

**Sanguinarine Chloride:** orange-red solid (72 mg, 98%); mp: 287-289 $^oC$ (lit.[15] 285-287 $^oC$). IR (KBr): ν =1684 $cm^{-1}$ ($C=N^+$). $^1H$ NMR (dmso-$d_6$, 400 MHz) δ: 10.14 (s, 1H), 8.75 (d, *J* =8.8 Hz, 1H), 8.62 (d, *J* =8.4 Hz, 1H), 8.28 (d, *J* =9.6 Hz, 1H), 8.11 (d, *J* =8.8 Hz, 1H), 7.76 (s, 1H), 6.61 (s, 2H), 6.35 (s, 2H), 4.93 (s, 3H). $^{13}C$ NMR (dmso-$d_6$, 100 MHz) δ: 155.8, 149.9, 148.7, 147.5, 146.2, 132.1, 131.4, 131.3, 127.1, 125.6, 120.2, 119.9, 118.8, 117.3, 109.4, 105.7, 104.9, 104.2, 102.7, 52.1. HRMS (ESI): calcd for $[C_{20}H_{14}NO_4]^+$: 332.0917; found: 332.0911.

**Chelerythrine Chloride**: yellow solid (74 mg, 97%), mp: 202-204 $^oC$ (lit.[15] 192-193 $^oC$). IR (KBr): ν =1678 $cm^{-1}$ ($C=N^+$). $^1H$ NMR (dmso-$d_6$, 400 MHz) δ: 10.11 (s, 1H), 8.84 (d, *J* =8.4 Hz, 2H), 8.30 (br s, 3H), 7.79 (s, 1H), 6.36 (s, 2H), 5.00 (s, 3H), 4.18 (s, 3H), 4.12 (s, 3H). $^{13}C$ NMR (dmso-$d_6$, 100 MHz) δ: 150.9, 150.6, 148.8, 148.7, 145.4, 132.3, 131.7, 131.1, 128.0, 126.1, 125.3, 120.1, 119.4, 119.2, 118.7, 105.8, 104.3, 102.7, 62.2, 57.0, 52.2. HRMS (ESI): calcd for $[C_{21}H_{18}NO_4]^+$: 348.1230; found: 348.1235.

**Nitidine Chloride**: yellow solid (74 mg, 97%); mp: 280-282 $^oC$ (lit.[15] 286-292 $^oC$). IR (KBr): ν =1684 $cm^{-1}$ ($C=N^+$). $^1H$ NMR (dmso-$d_6$, 400MHz) δ: 9.88 (s, 1H), 8.92 (d, *J* =8.8 Hz, 1H), 8.38 (s, 1H), 8.32 (s, 1H), 8.30 (d, *J* =8.8 Hz), 7.91 (s, 1H), 7.79 (s, 1H), 6.35 (s, 2H), 4.90 (s, 3H), 4.24 (s, 3H), 4.04 (s, 3H). $^{13}C$ NMR (dmso-$d_6$, 100 MHz) δ: 158.3, 151.5, 151.3, 148.9, 148.4, 132.6, 132.5, 130.0, 124.1, 119.9, 119.4, 119.3, 108.7, 105.7, 104.6, 103.3, 102.7, 57.3, 56.3, 51.4. HRMS (ESI): calcd for $[C_{21}H_{18}NO_4]^+$: 348.1230; found: 348.1234.

**Avicine Chloride**: yellow solid (74 mg, 97%); mp: 338-342 $^oC$ . IR (KBr): ν =1684 $cm^{-1}$ ($C=N^+$). $^1H$ NMR (dmso-$d_6$, 400 MHz) δ: 9.89 (s, 1H), 8.73 (d, *J* =8.4 Hz, 1H), 8.59 (s, 1H), 8.31 (s, 1H), 8.24 (d, *J* =8.4 Hz, 1H), 7.86 (s, 1H), 7.76 (s, 1H), 6.49 (s, 2H), 6.36 (s, 2H), 4.89 (s, 3H). $^{13}C$ NMR (100 MHz,

$CDCl_3$) δ: 157.2, 151.4, 150.2, 149.0, 148.5, 134.6, 132.8, 132.6, 130.2, 124.6, 120.8, 119.8, 119.1, 105.7, 105.7, 104.6, 104.2, 102.8, 100.9, 51.4. HRMS (ESI): calcd for $[C_{20}H_{14}NO_4]^+$: 332.0917; found: 332.0920.

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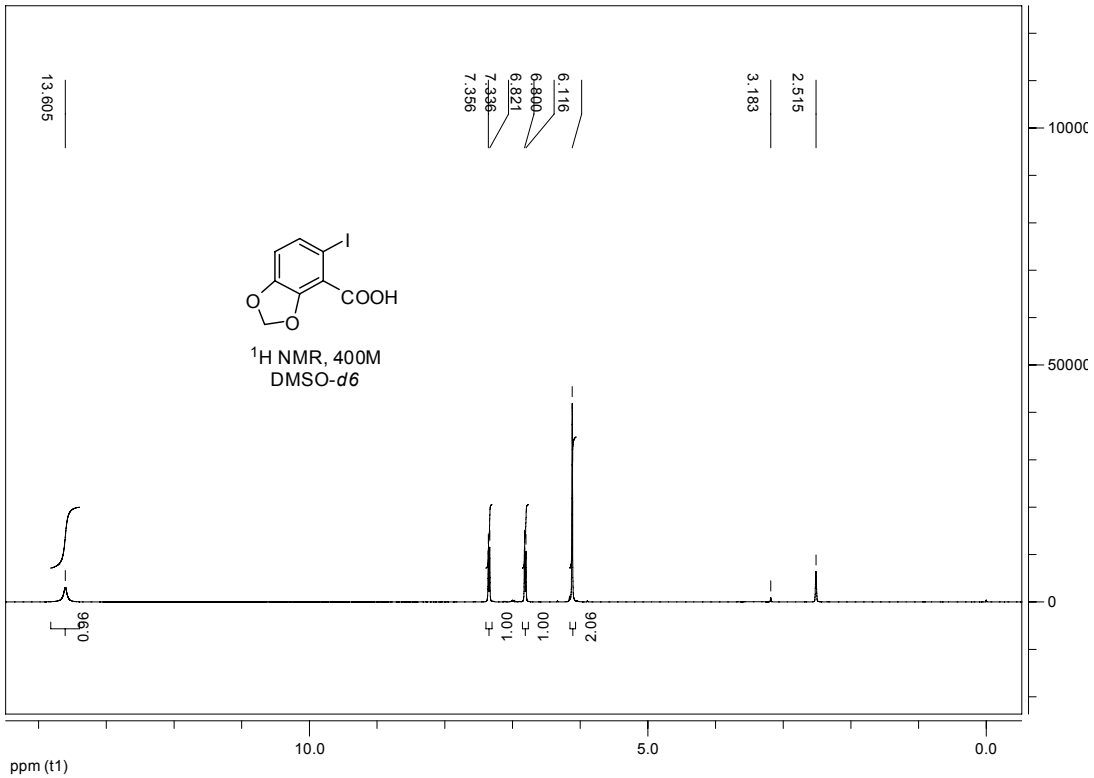
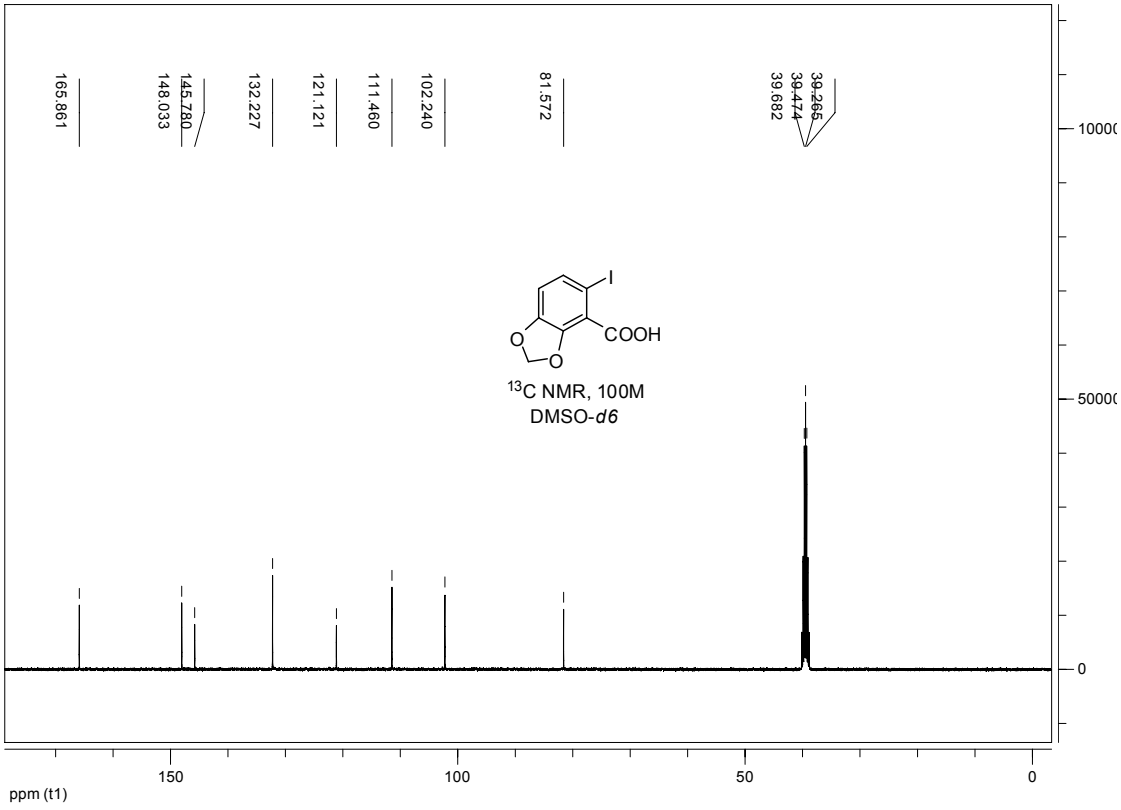
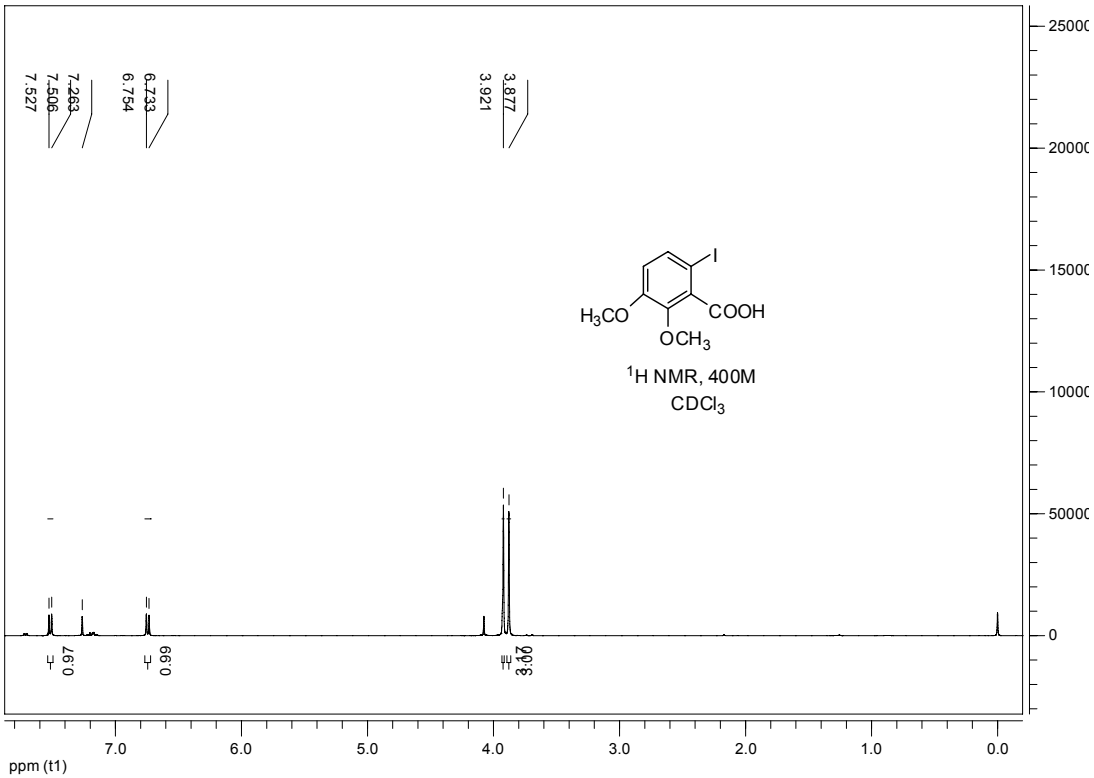
## Part 2. NMR Spectra of All Compounds

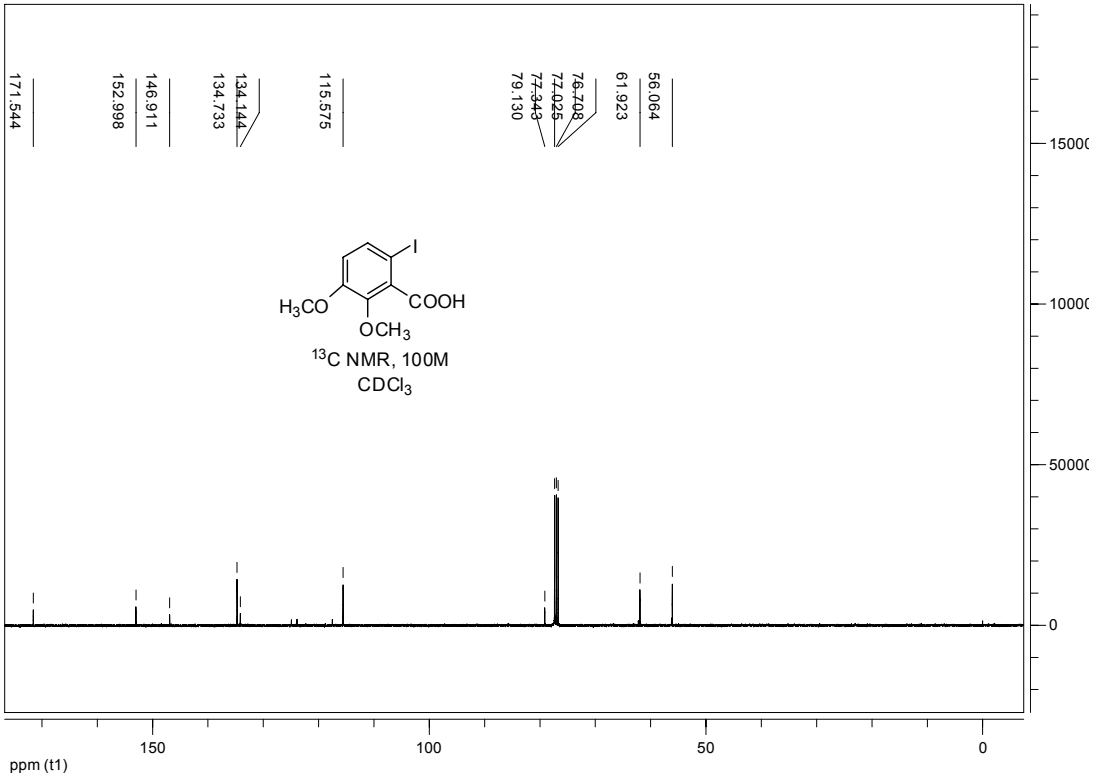
### 12a


13.605
7.356
7.336
6.821
6.800
6.116
3.183
2.515
I
COOH
O
O
$^1$H NMR, 400M
DMSO-*d6*
0.96
1.00
1.00
2.06
10000
5000
0
10.0
5.0
0.0
ppm (t1)

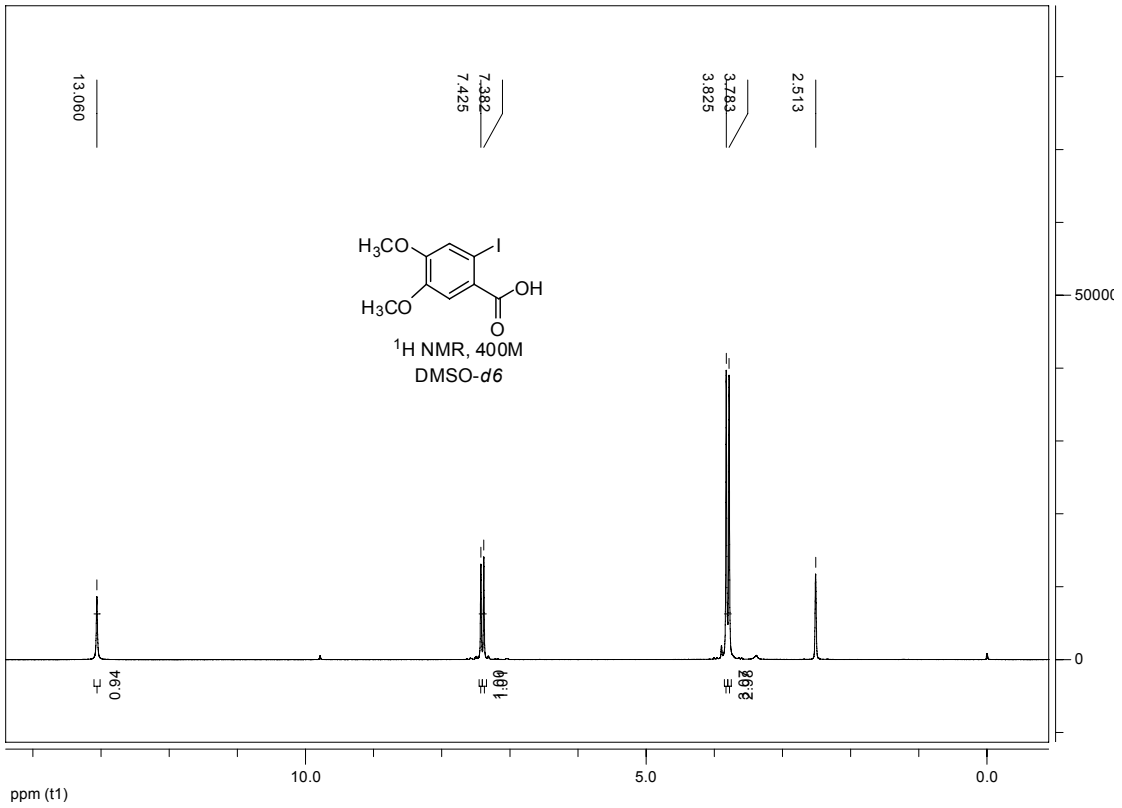

165.861
148.033
145.780
132.227
121.121
111.460
102.240
81.572
39.682
39.474
39.265
I
COOH
O
O
$^{13}$C NMR, 100M
DMSO-*d6*
10000
5000
0
150
100
50
0
ppm (t1)

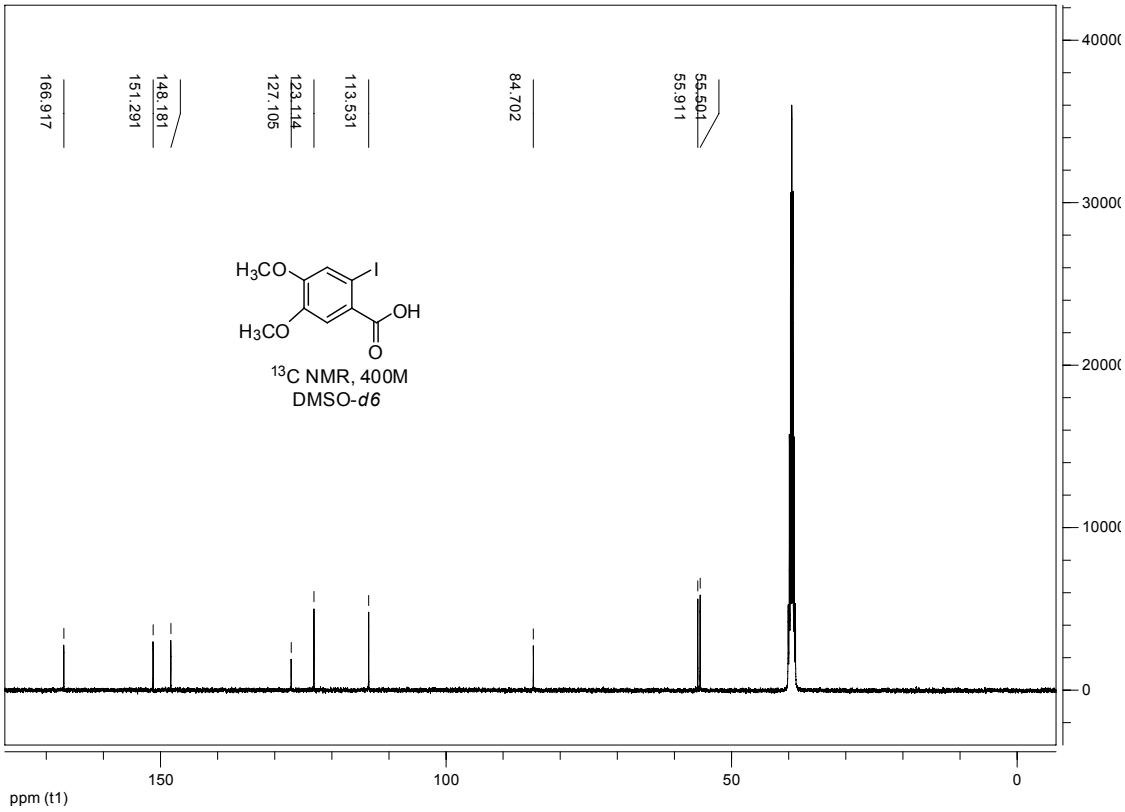
**12b**


7.527
7.506
7.263
6.754
6.733
3.921
3.877
I
H3CO
COOH
OCH3
1H NMR, 400M
CDCl3
0.97
0.99
3.00
ppm (t1)

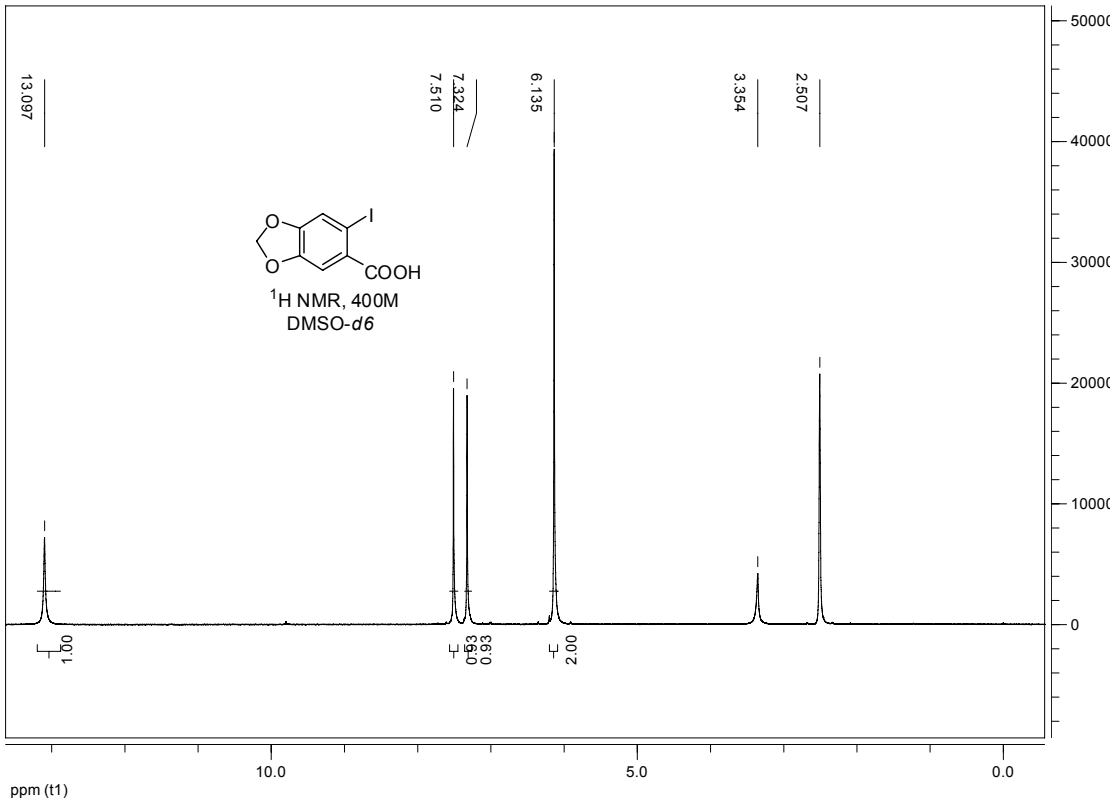

171.544
152.998
146.911
134.733
134.144
115.575
79.130
77.343
77.025
76.708
61.923
56.064
I
H3CO
COOH
OCH3
13C NMR, 100M
CDCl3
ppm (t1)

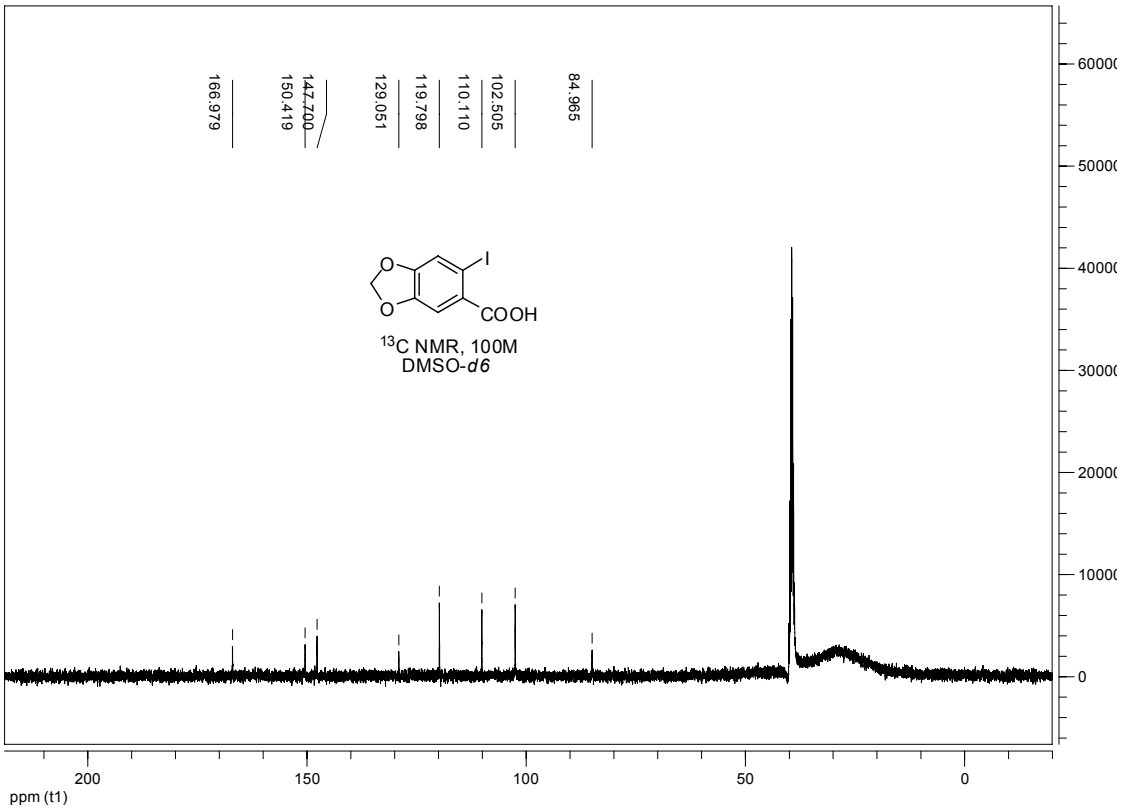
**12c**


13.060
7.425
7.382
3.825
3.783
2.513
H3CO
I
OH
H3CO
O
1H NMR, 400M
DMSO-d6
0.94
1.00
2.98
50000
0
10.0
5.0
0.0
ppm (t1)

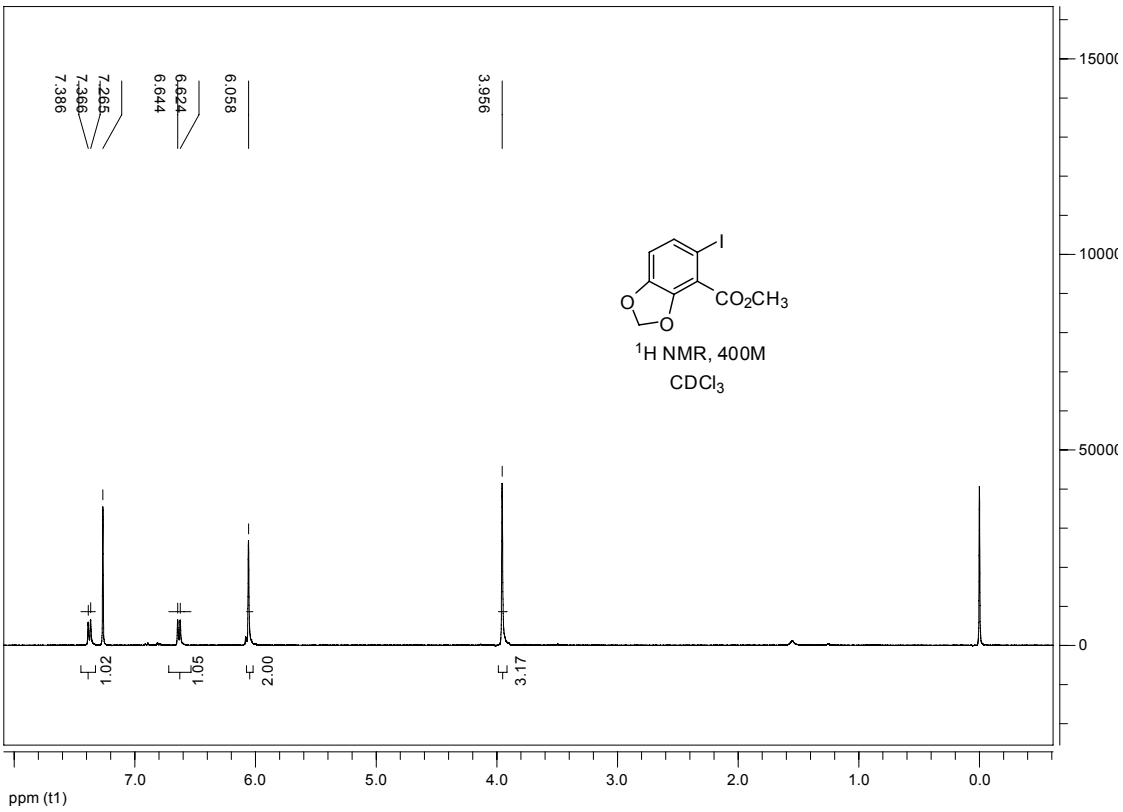

166.917
151.291
148.181
127.105
123.114
113.531
84.702
55.911
55.501
H3CO
I
OH
H3CO
O
13C NMR, 400M
DMSO-d6
40000
30000
20000
10000
0
150
100
50
0
ppm (t1)

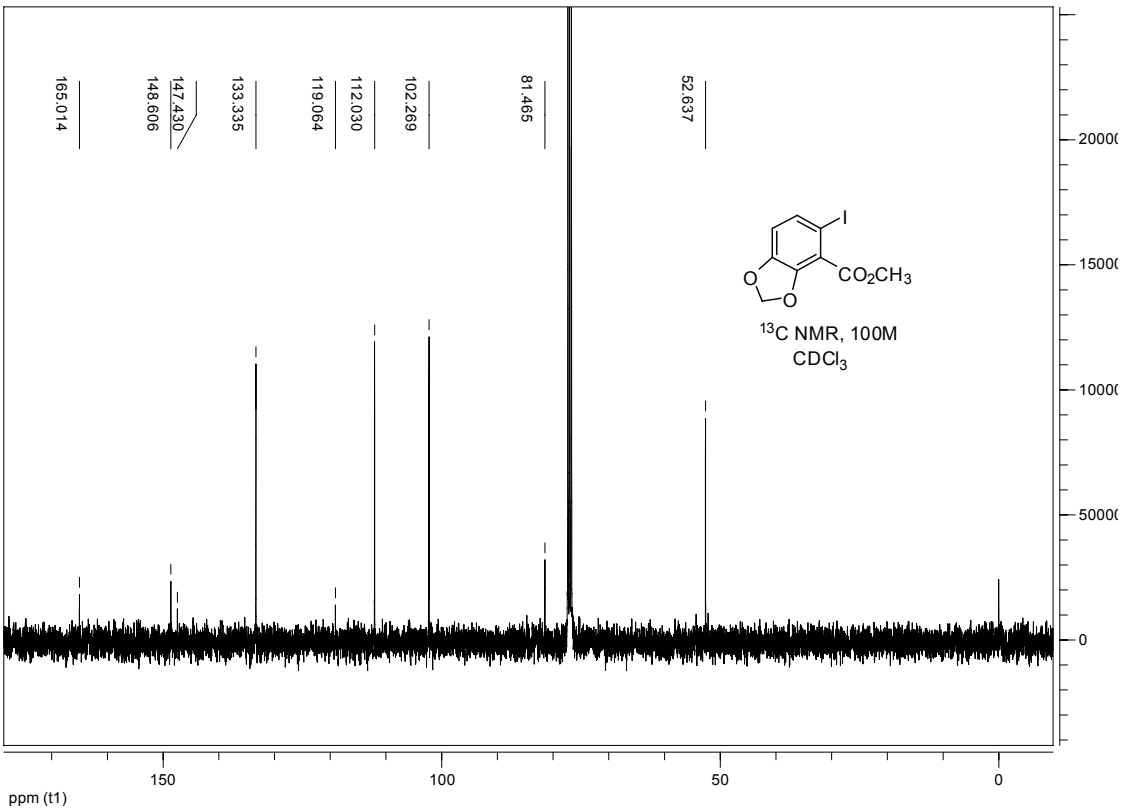
**12d**


13.097
7.510
7.324
6.135
3.354
2.507
I
O
O
COOH
$^{1}$H NMR, 400M
DMSO-*d6*
1.00
0.93
0.93
2.00
10.0
5.0
0.0
ppm (t1)

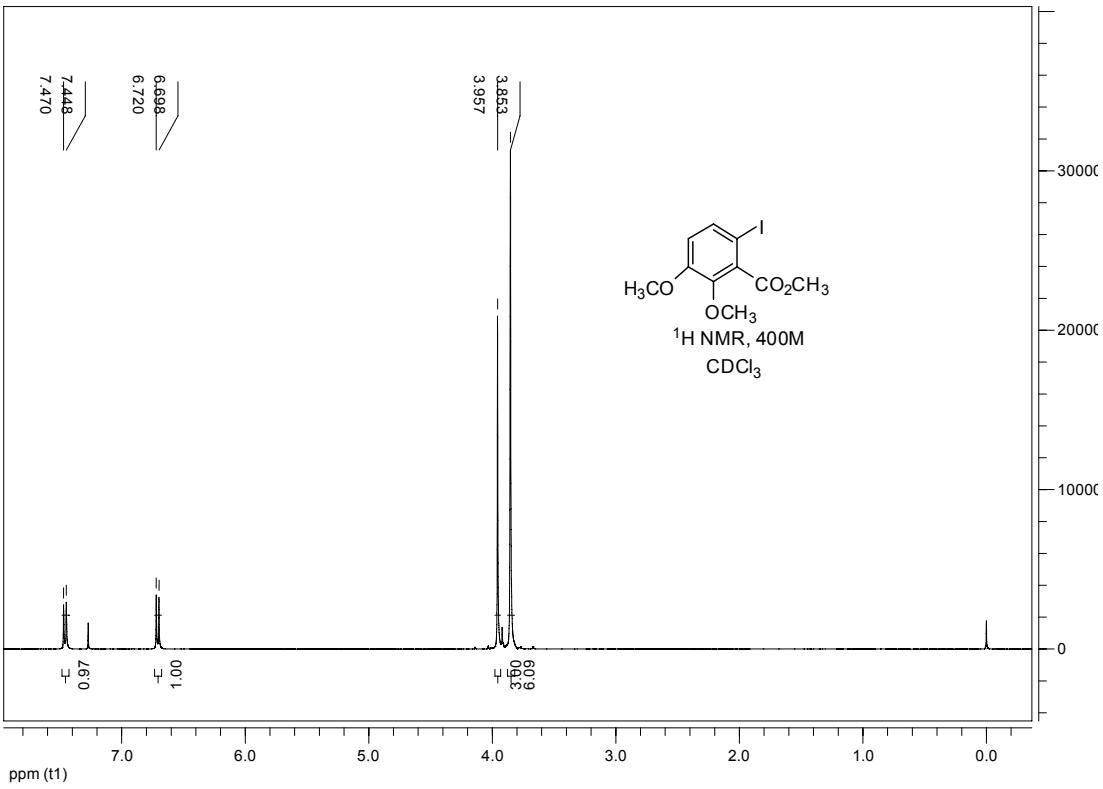

166.979
150.419
147.700
129.051
119.798
110.110
102.505
84.965
I
O
O
COOH
$^{13}$C NMR, 100M
DMSO-*d6*
200
150
100
50
0
ppm (t1)

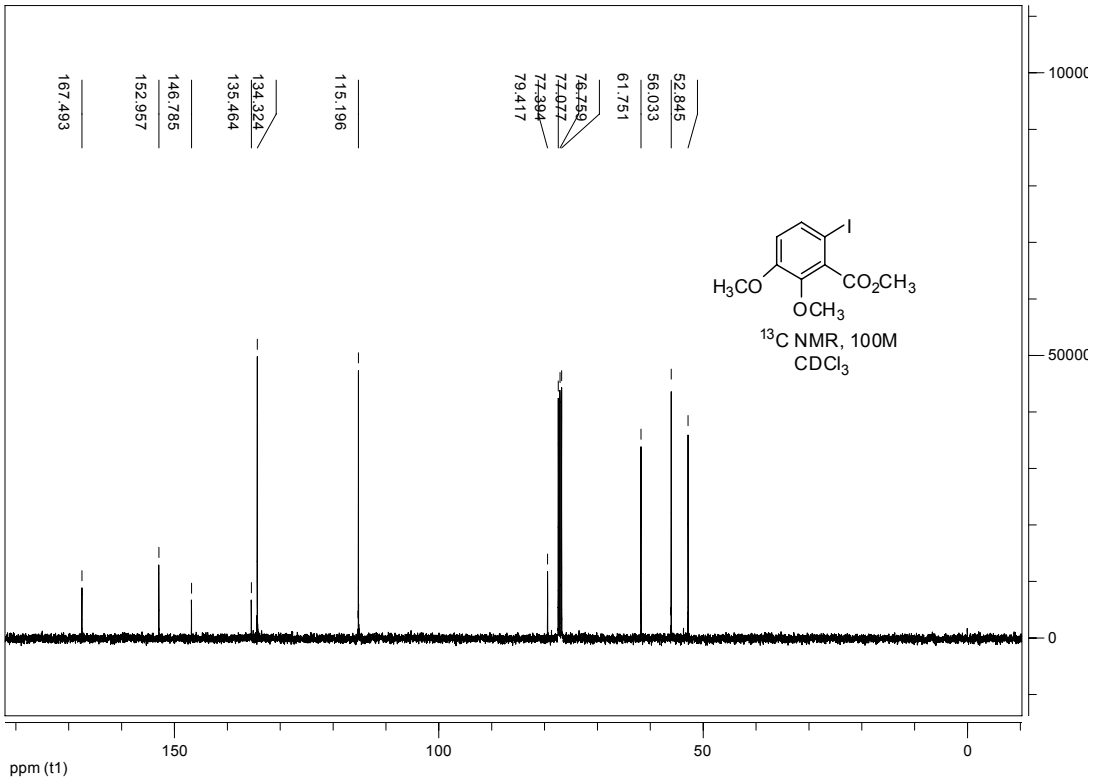
**13a**


7.386
7.366
7.265
6.644
6.624
6.058
3.956
I
O
O
CO2CH3
1H NMR, 400M
CDCl3
1.02
1.05
2.00
3.17
ppm (t1)

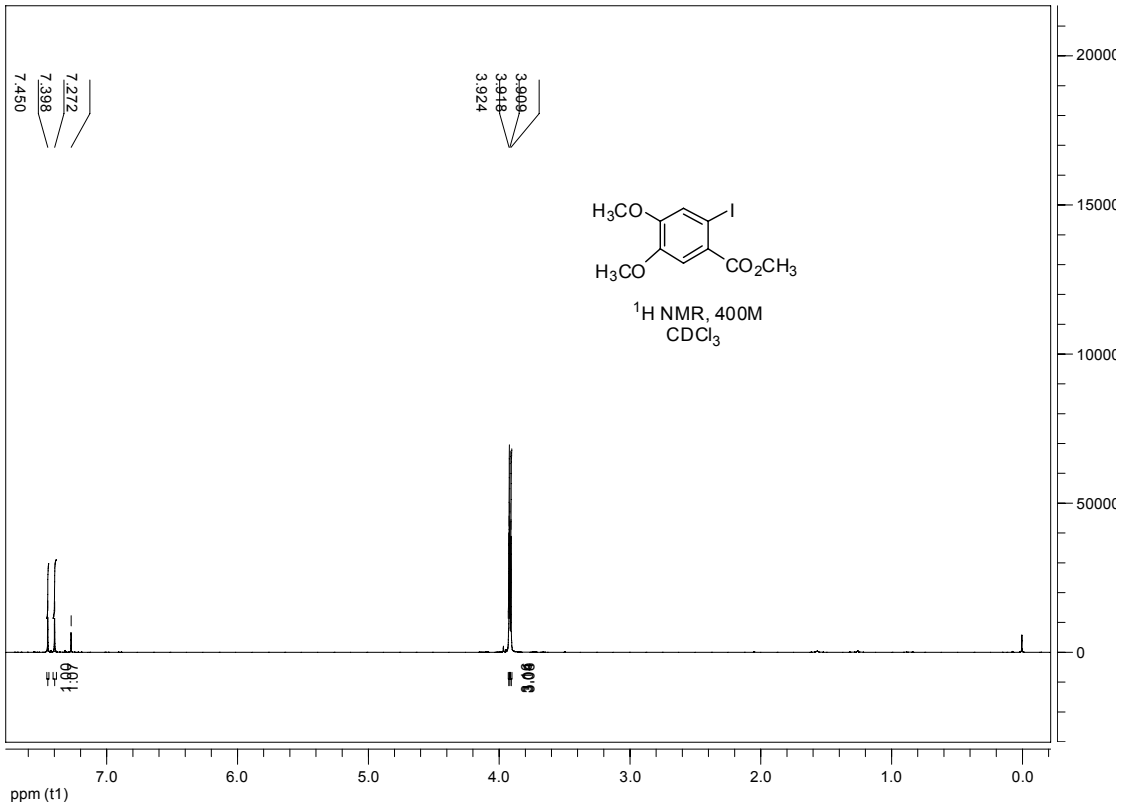

165.014
148.606
147.430
133.335
119.064
112.030
102.269
81.465
52.637
I
O
O
CO2CH3
13C NMR, 100M
CDCl3
ppm (t1)

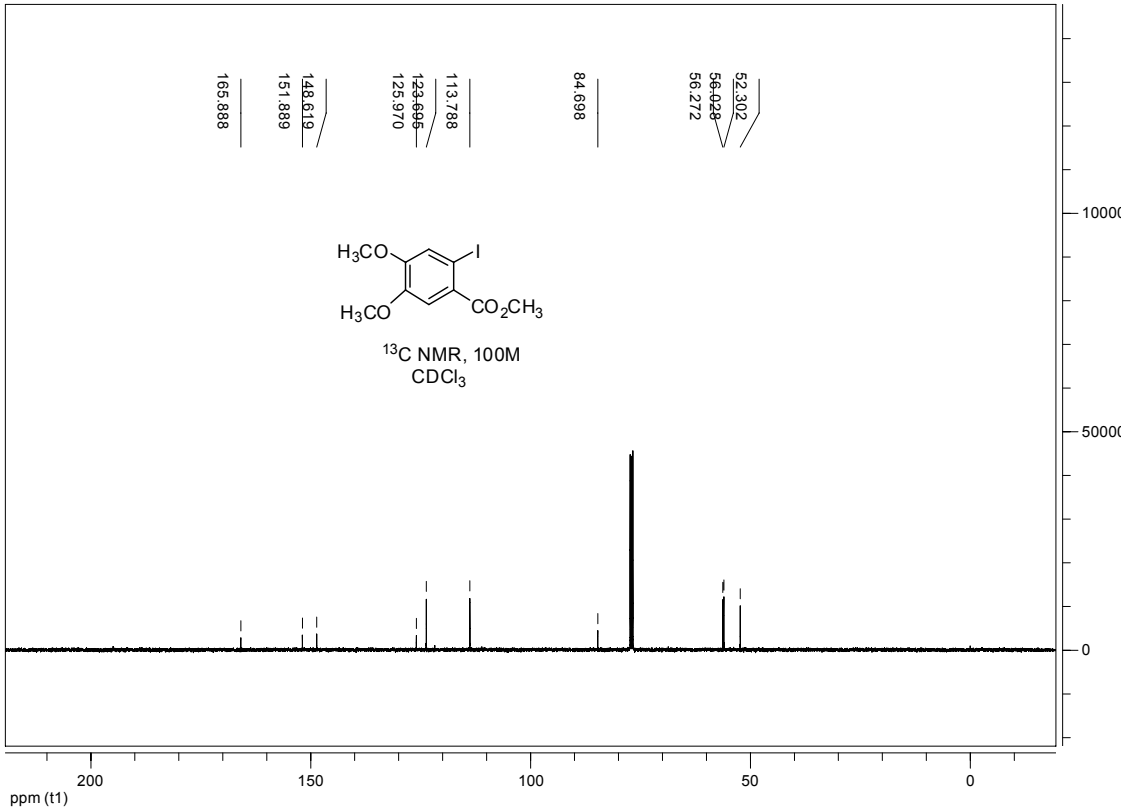
**13b**


7.470
7.448
6.720
6.698
3.957
3.853
0.97
1.00
6.09
3.00
I
H3CO
CO2CH3
OCH3
1H NMR, 400M
CDCl3
ppm (t1)

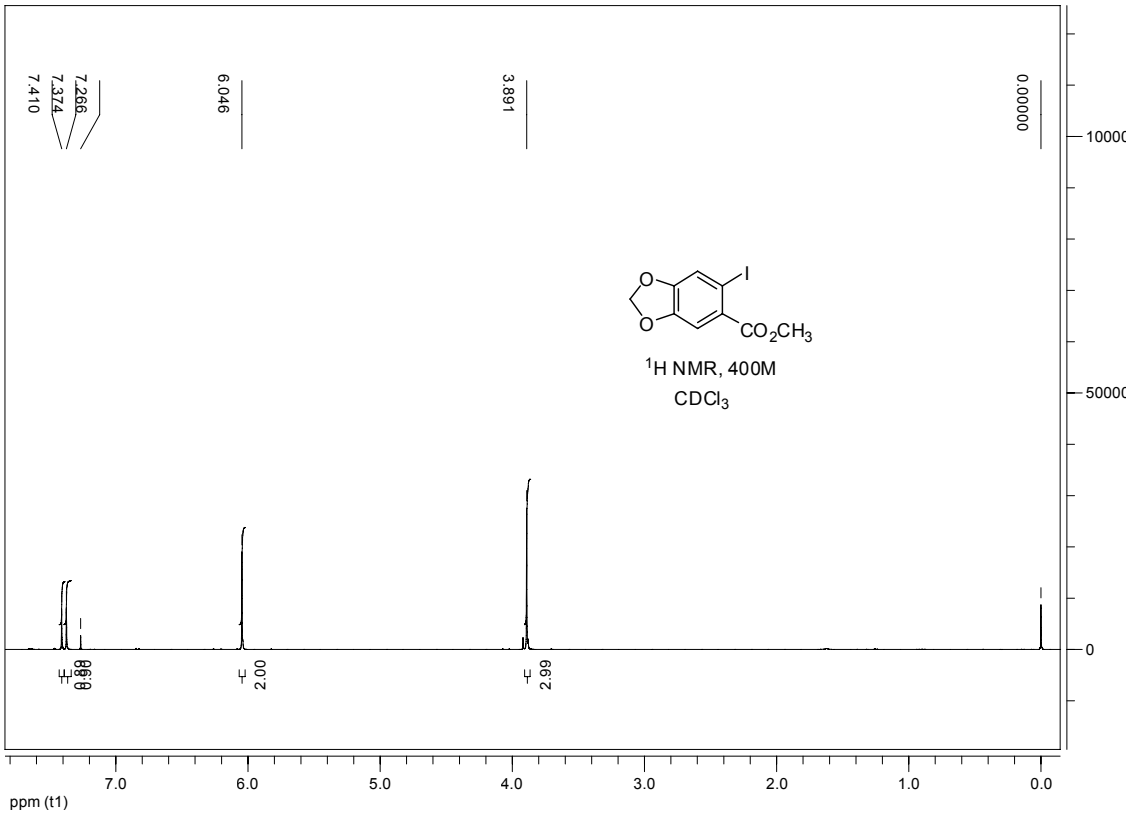

167.493
152.957
146.785
135.464
134.324
115.196
79.417
77.394
77.077
76.759
61.751
56.033
52.845
I
H3CO
CO2CH3
OCH3
13C NMR, 100M
CDCl3
ppm (t1)

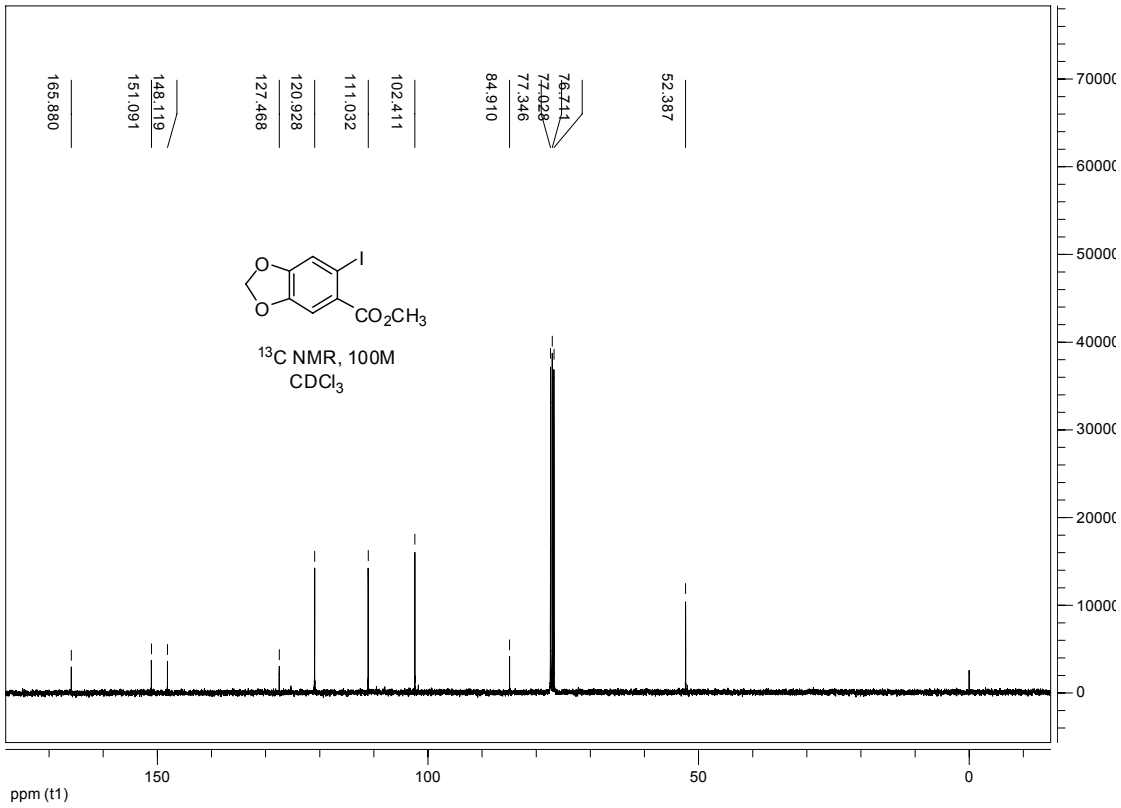
**13c**


7.450
7.398
7.272
3.924
3.918
3.909
H3CO
I
H3CO
CO2CH3
1H NMR, 400M
CDCl3
20000
15000
10000
5000
0
1.00
3.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

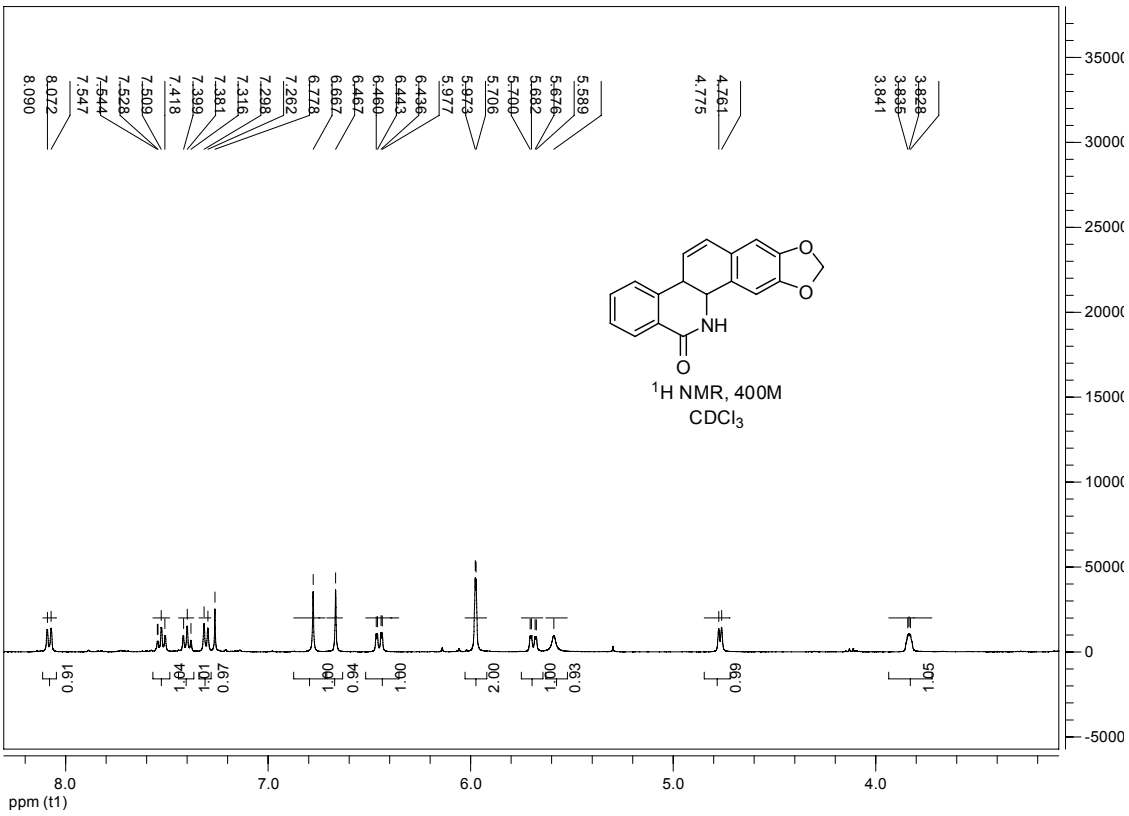

165.888
151.889
148.619
125.970
123.695
113.788
84.698
56.272
56.028
52.302
H3CO
I
H3CO
CO2CH3
13C NMR, 100M
CDCl3
10000
5000
0
200
150
100
50
0
ppm (t1)

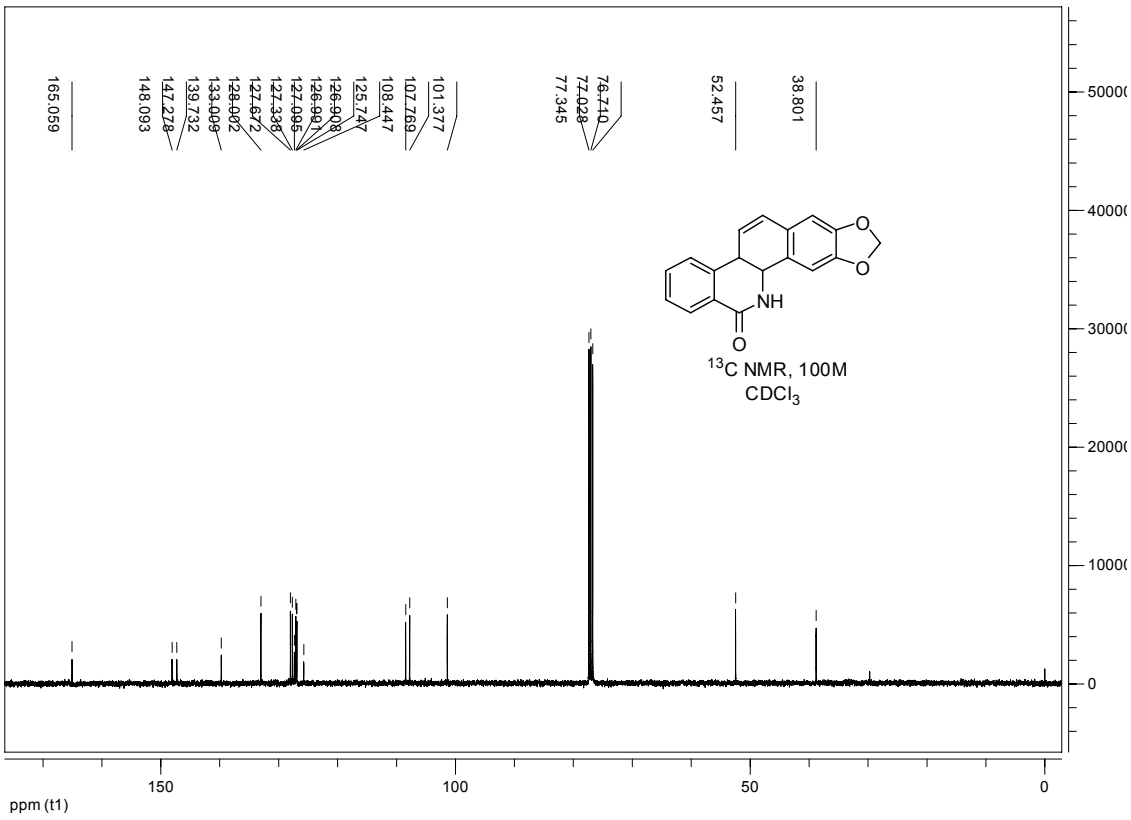
**13d**


7.410
7.374
7.266
6.046
3.891
0.00000
2.00
2.99
I
O
O
CO2CH3
1H NMR, 400M
CDCl3
ppm (t1)

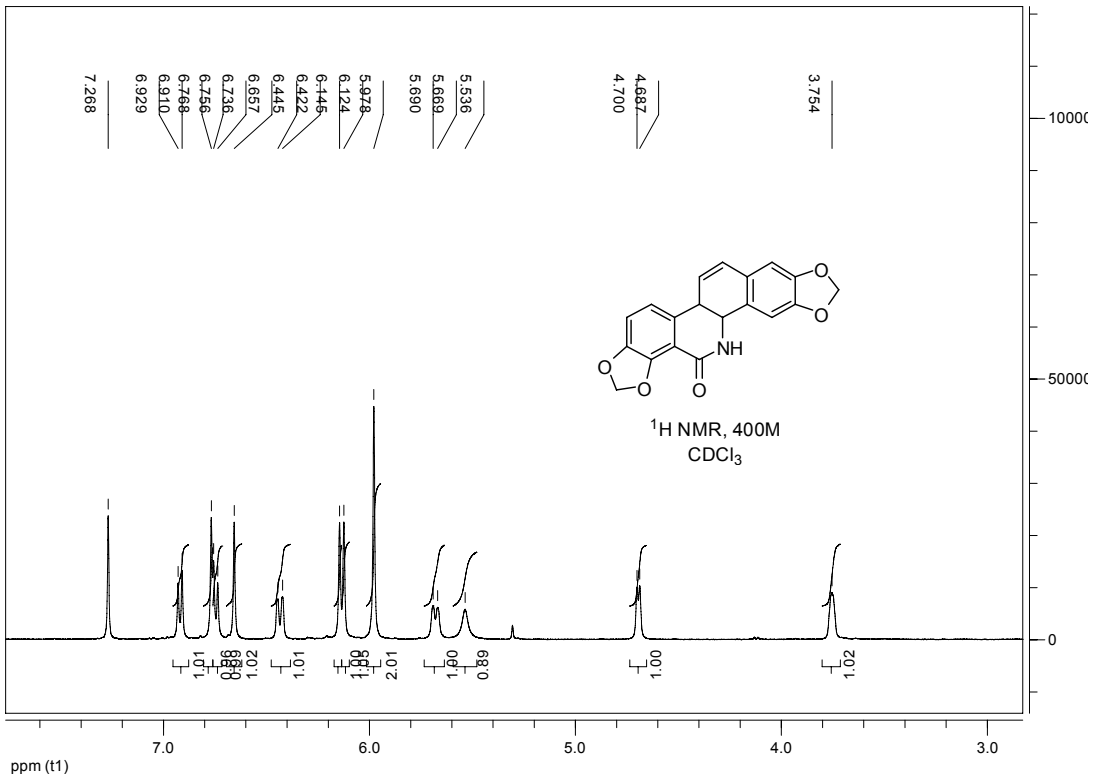

165.880
151.091
148.119
127.468
120.928
111.032
102.411
84.910
77.346
77.028
76.711
52.387
I
O
O
CO2CH3
13C NMR, 100M
CDCl3
ppm (t1)

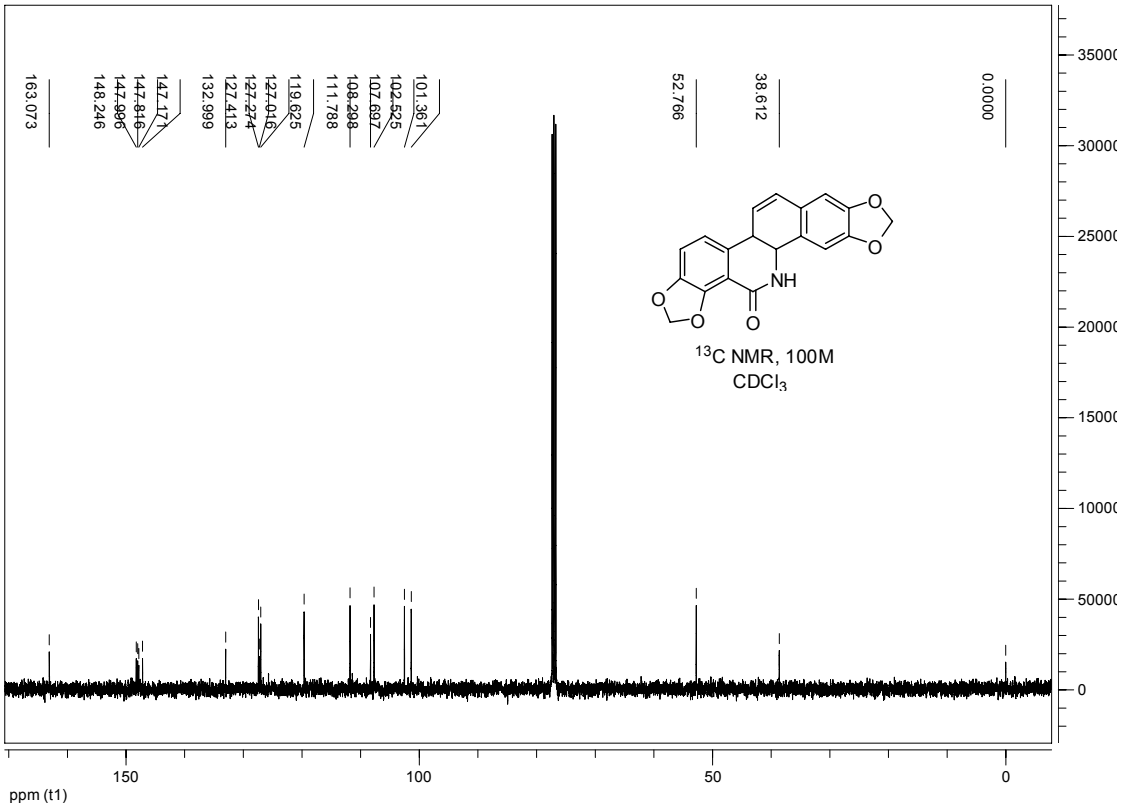
**10**


8.090
8.072
7.547
7.544
7.528
7.509
7.418
7.399
7.381
7.316
7.298
7.262
6.778
6.667
6.467
6.460
6.443
6.436
5.977
5.973
5.706
5.700
5.682
5.676
5.589
4.775
4.761
3.841
3.835
3.828
O
O
NH
O
$^1$H NMR, 400M
$CDCl_3$
0.91
1.64
1.01
0.97
1.00
0.94
1.00
2.00
1.00
0.93
0.99
1.05
8.0
7.0
6.0
5.0
4.0
ppm (t1)

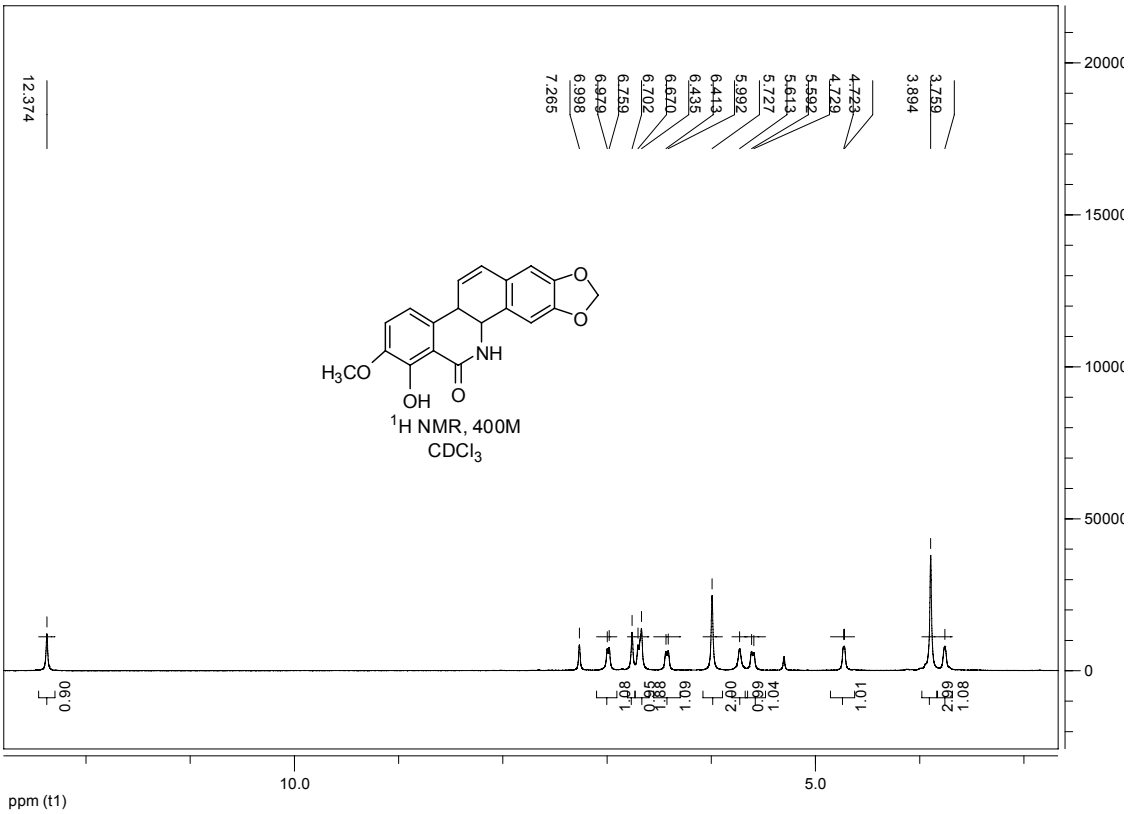

165.059
148.093
147.278
139.732
133.009
128.002
127.672
127.338
127.095
126.991
126.908
125.747
108.447
107.769
101.377
77.345
77.028
76.710
52.457
38.801
O
O
NH
O
$^{13}$C NMR, 100M
$CDCl_3$
150
100
50
0
ppm (t1)

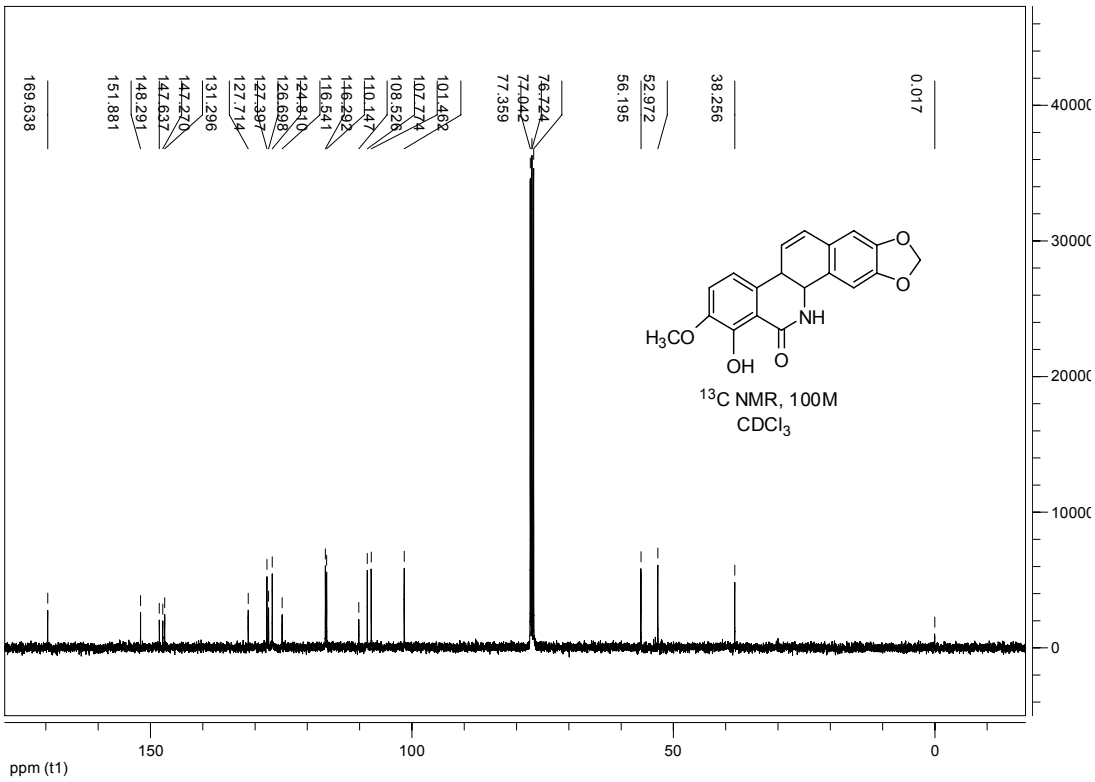
**16a**


7.268
6.929
6.910
6.768
6.756
6.736
6.657
6.445
6.422
6.145
6.124
5.978
5.690
5.669
5.536
4.700
4.687
3.754
NH
O
O
O
O
O
1H NMR, 400M
CDCl3
ppm (t1)

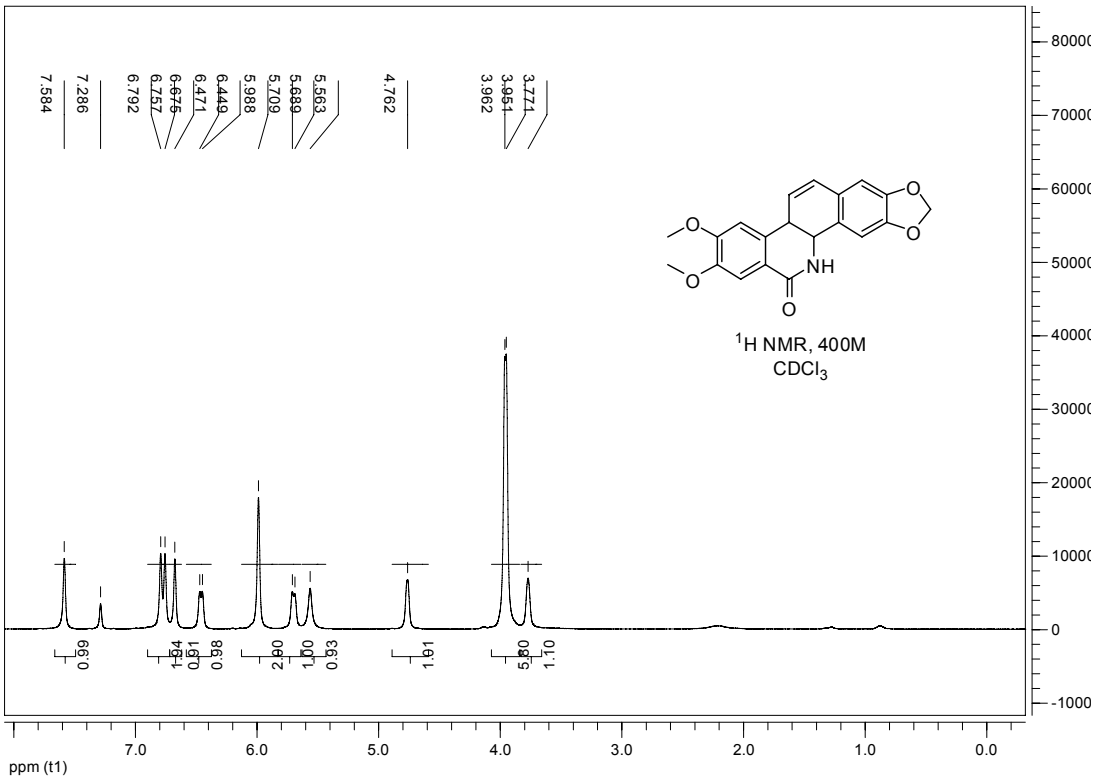

163.073
148.246
147.996
147.816
147.171
132.999
127.413
127.274
127.016
119.625
111.788
108.298
107.697
102.525
101.361
52.766
38.612
0.0000
NH
O
O
O
O
O
13C NMR, 100M
CDCl3
ppm (t1)

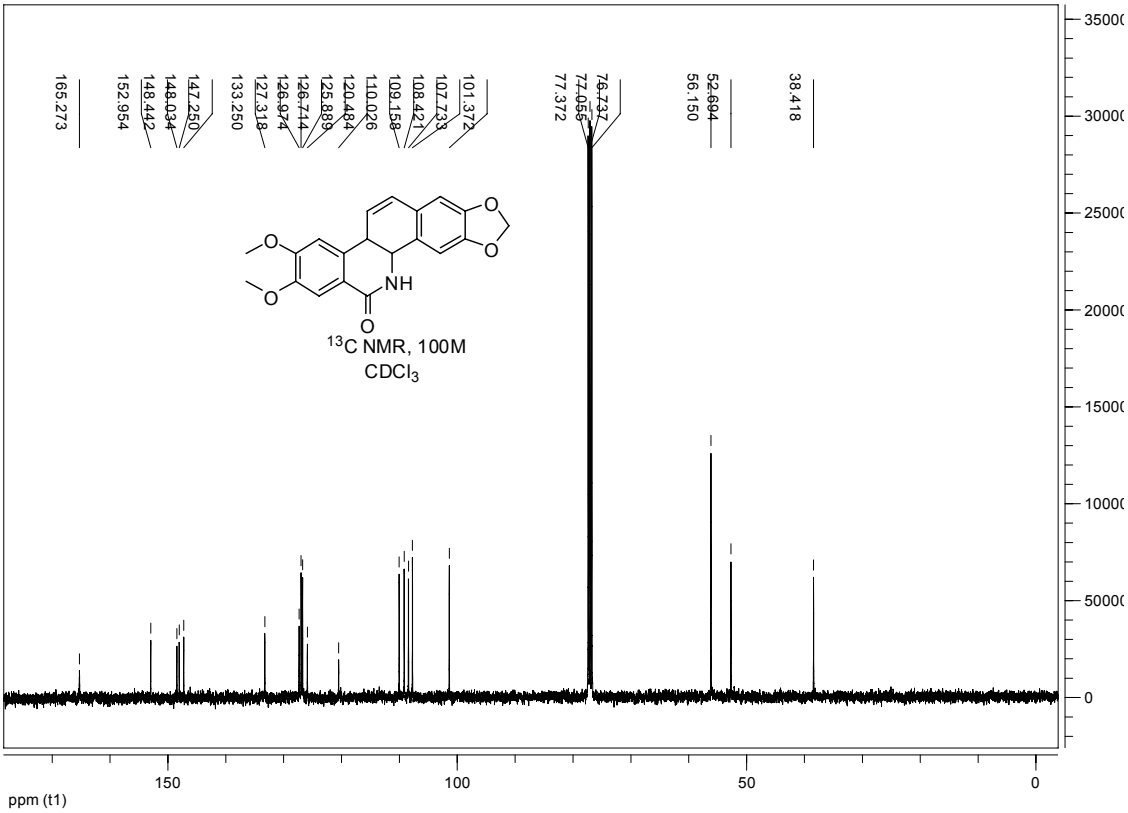
**16b**



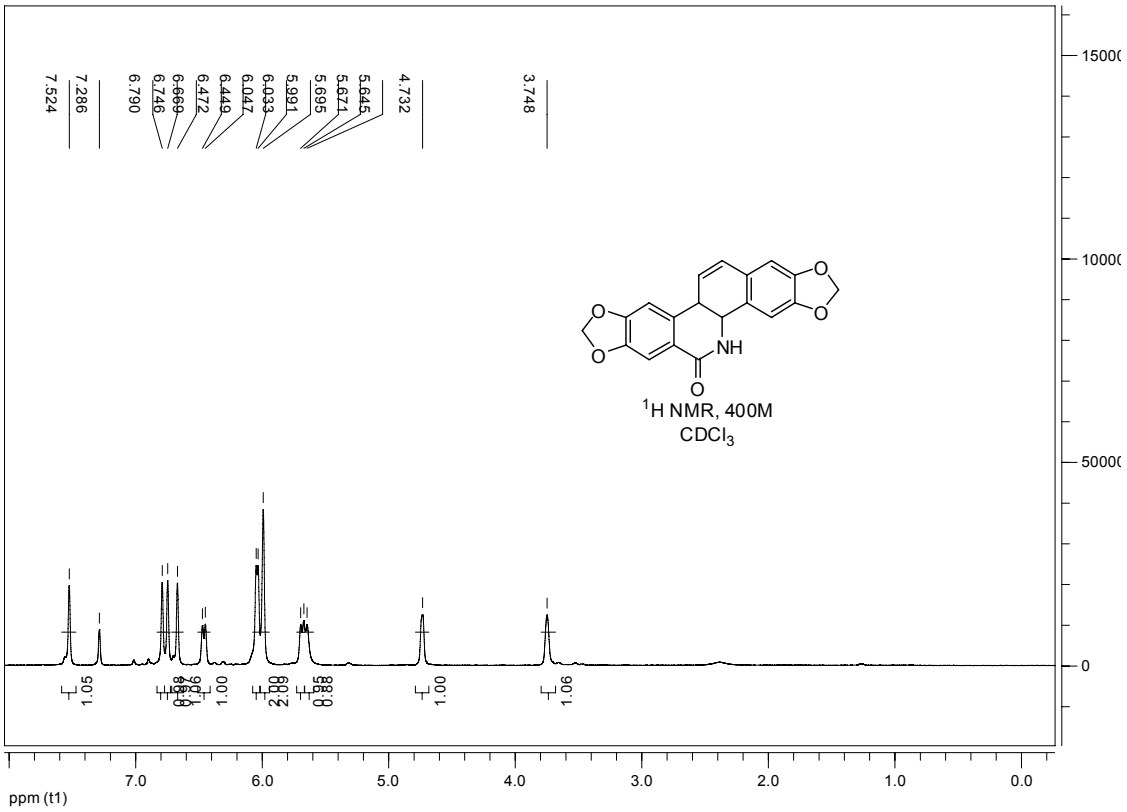



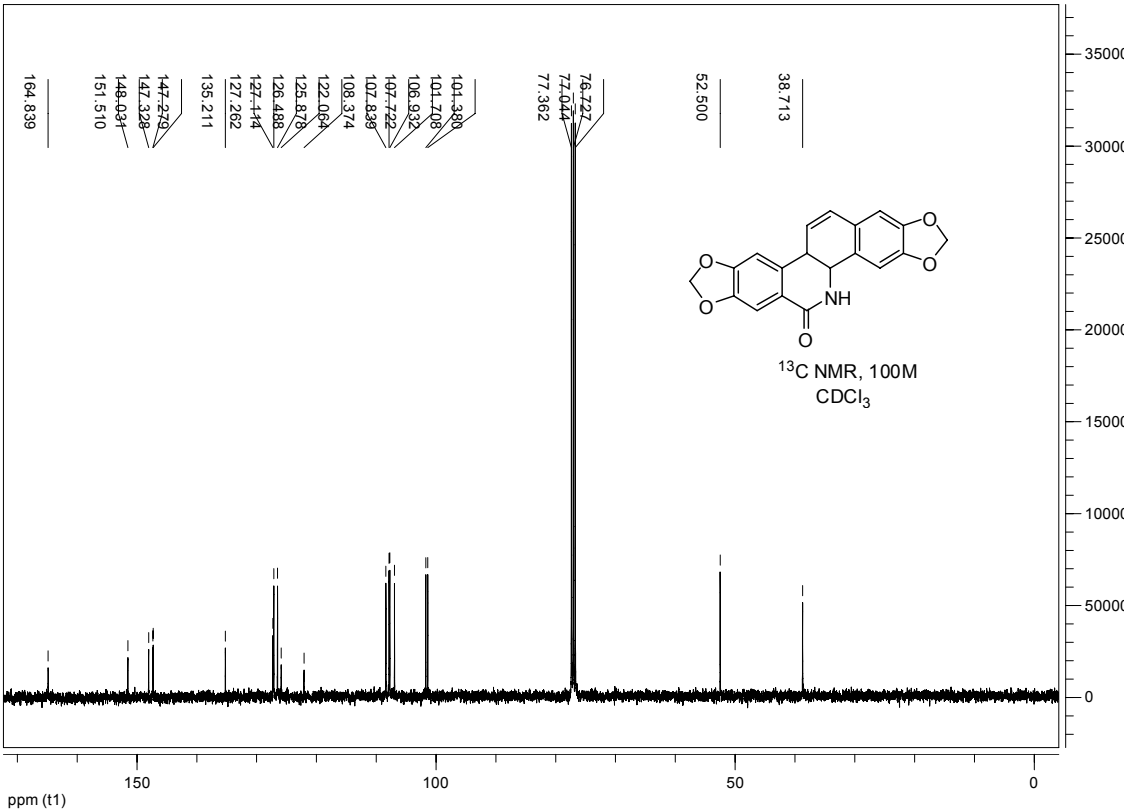

**16c**



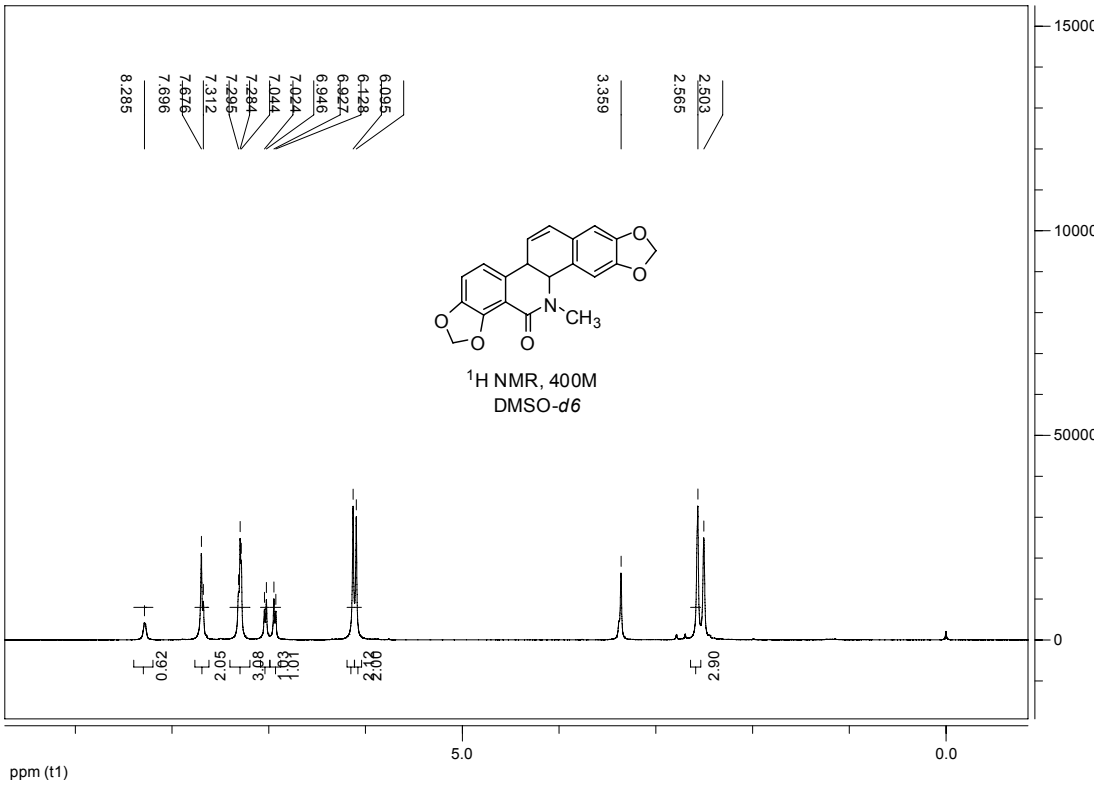



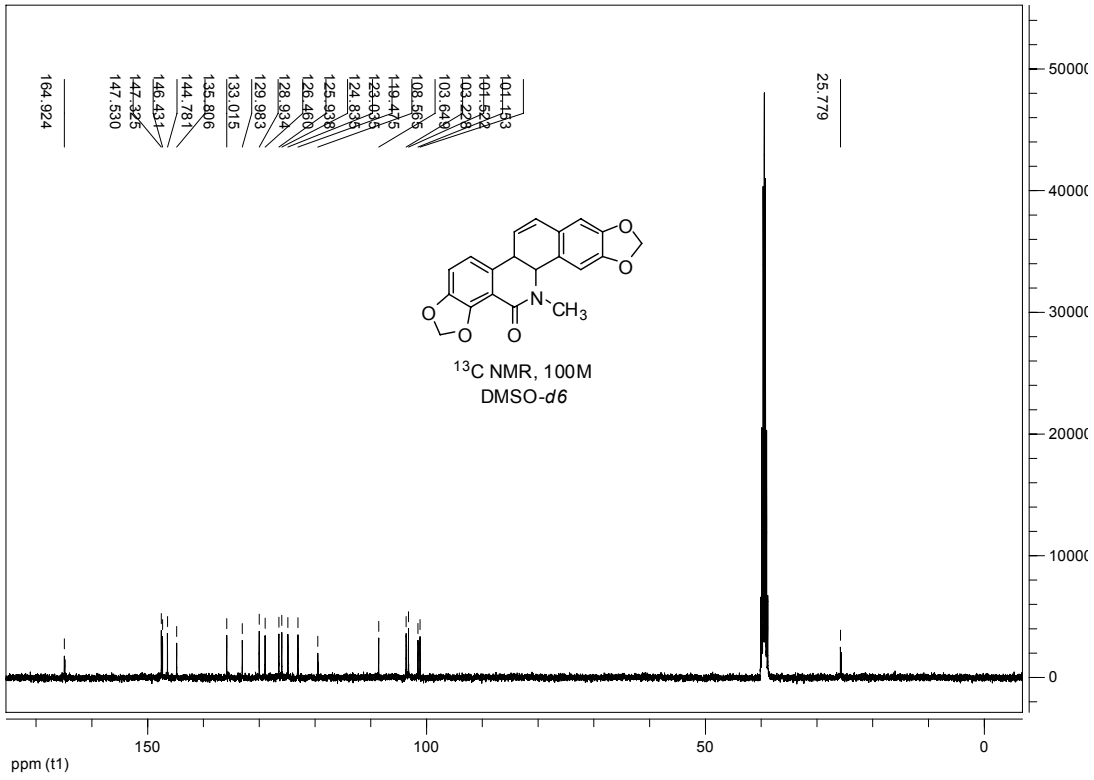

**16d**


7.524
7.286
6.790
6.746
6.669
6.472
6.449
6.047
6.033
5.991
5.695
5.671
5.645
4.732
3.748
NH
O
$^{1}$H NMR, 400M
$CDCl_3$
ppm (t1)

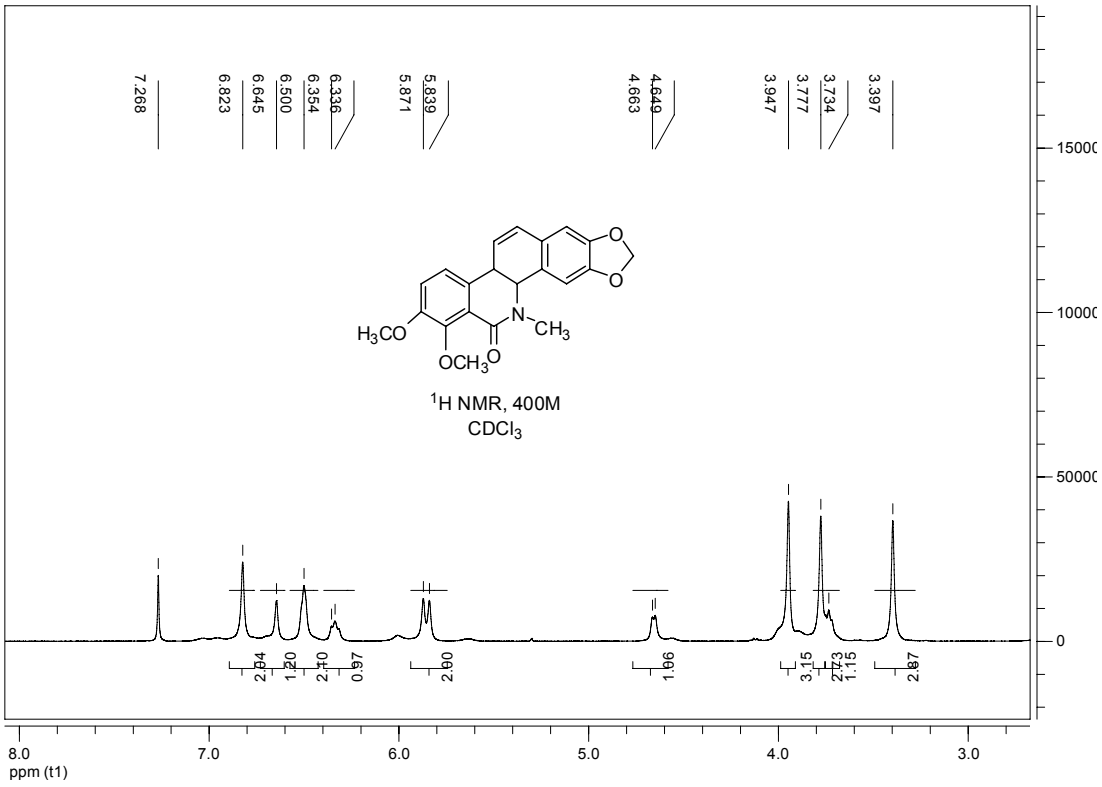

164.839
151.510
149.031
147.328
147.279
135.211
127.262
127.114
126.488
125.878
122.064
108.374
107.839
107.722
106.932
101.708
101.380
77.362
77.041
76.727
52.500
38.713
NH
O
$^{13}$C NMR, 100M
$CDCl_3$
ppm (t1)

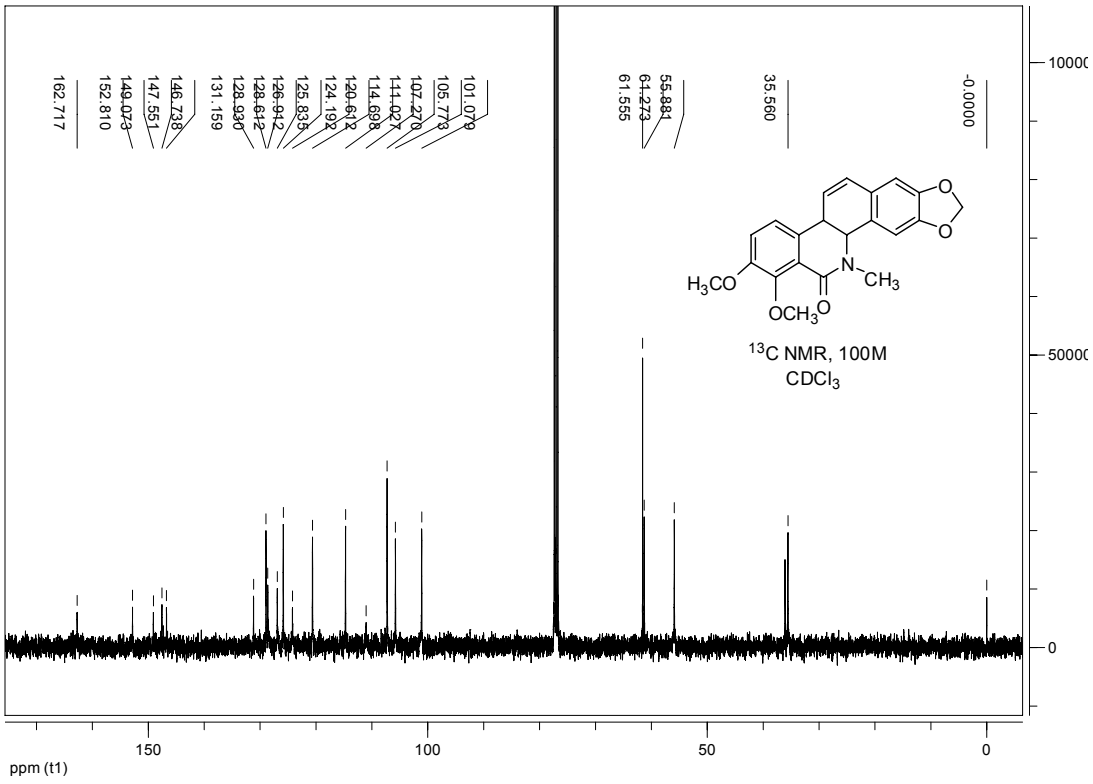
**17a**


8.285
7.696
7.676
7.312
7.295
7.284
7.044
7.024
6.946
6.927
6.128
6.095
3.359
2.565
2.503
O
O
O
O
O
N
CH3
1H NMR, 400M
DMSO-d6
0.62
2.05
3.08
1.83
2.00
2.20
2.90
15000
10000
5000
0
5.0
0.0
ppm (t1)

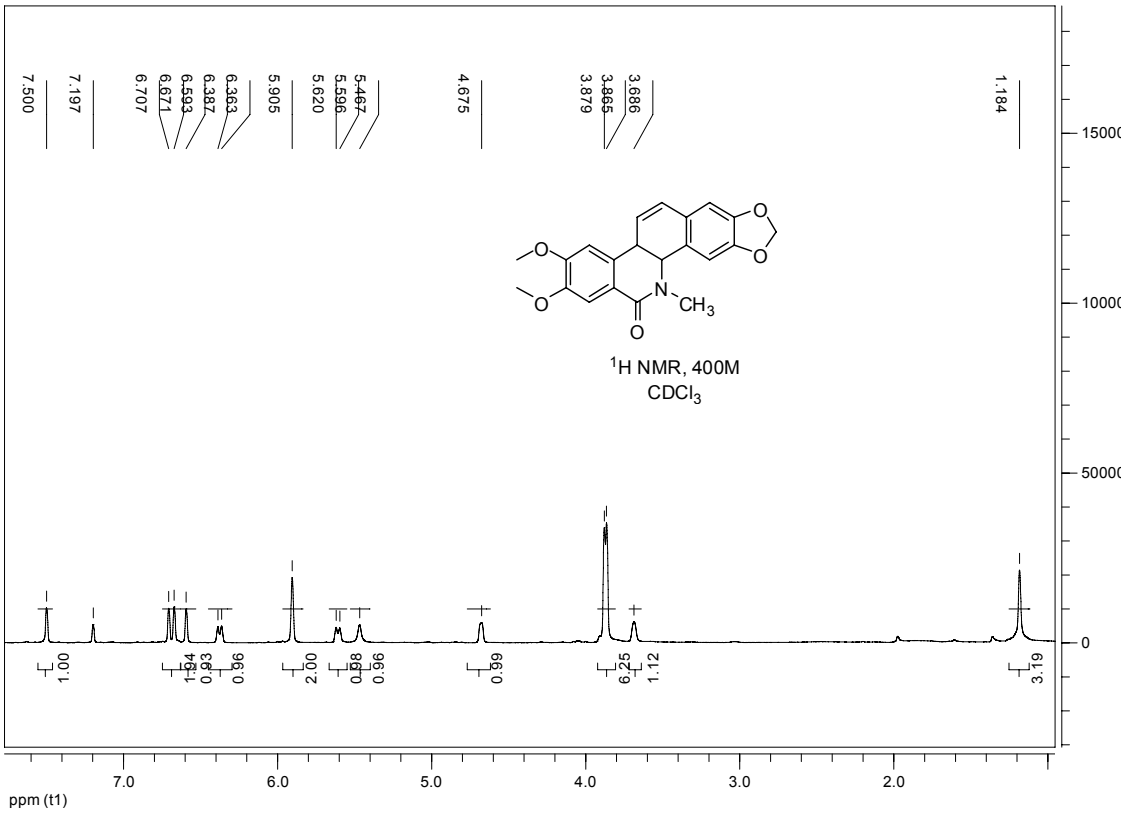

164.924
147.530
147.325
146.431
144.781
135.806
133.015
129.983
128.934
126.460
125.908
124.835
123.035
119.475
108.565
103.649
103.228
101.522
101.183
25.779
O
O
O
O
O
N
CH3
13C NMR, 100M
DMSO-d6
50000
40000
30000
20000
10000
0
150
100
50
0
ppm (t1)

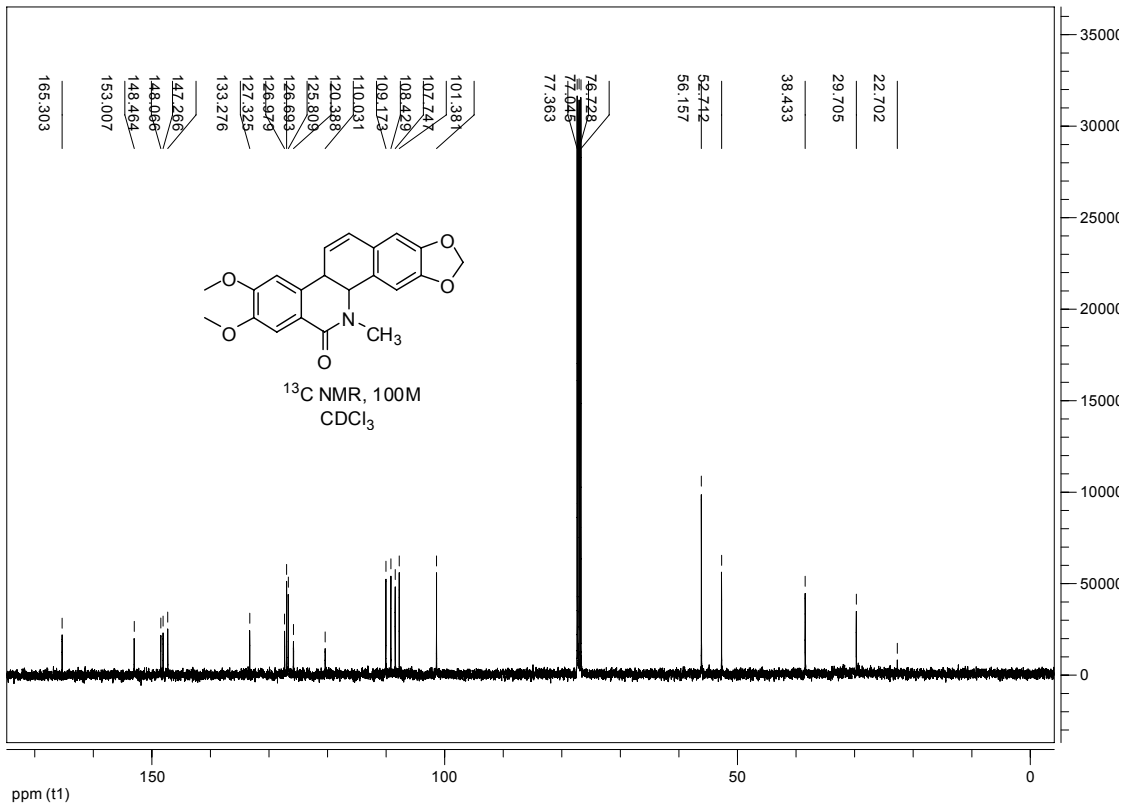
**17b**



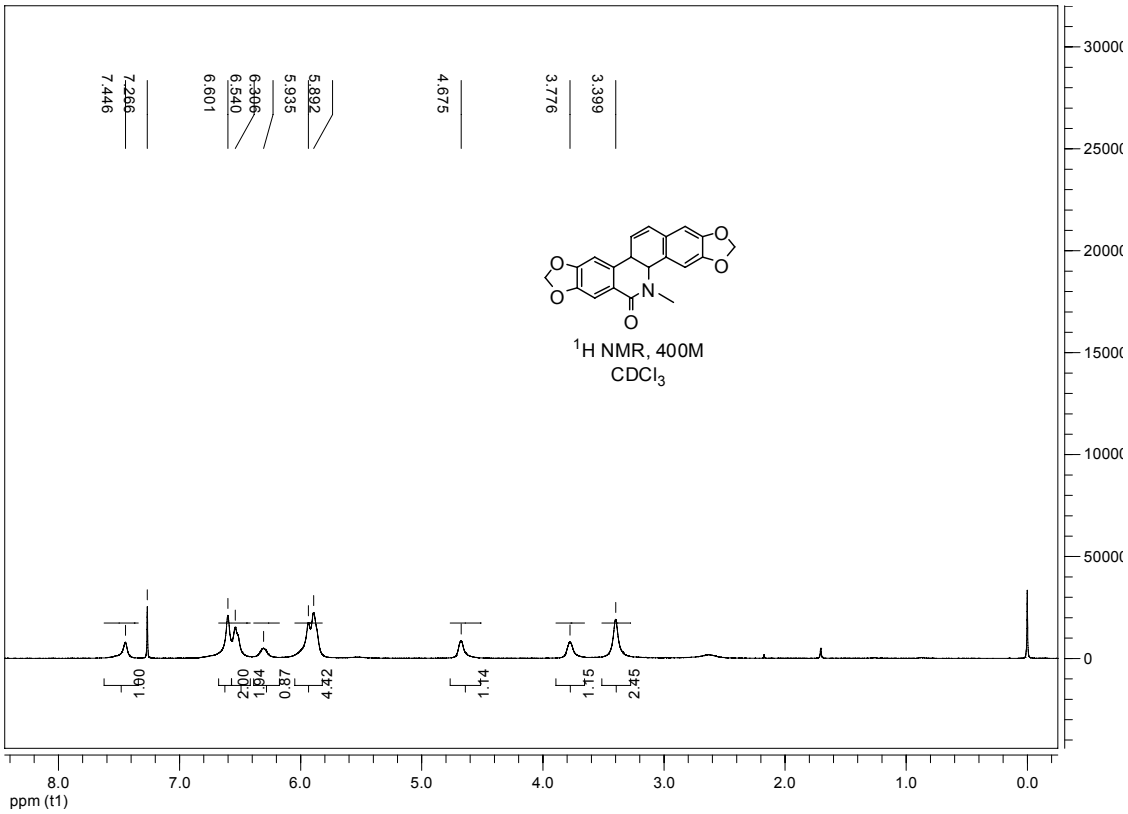



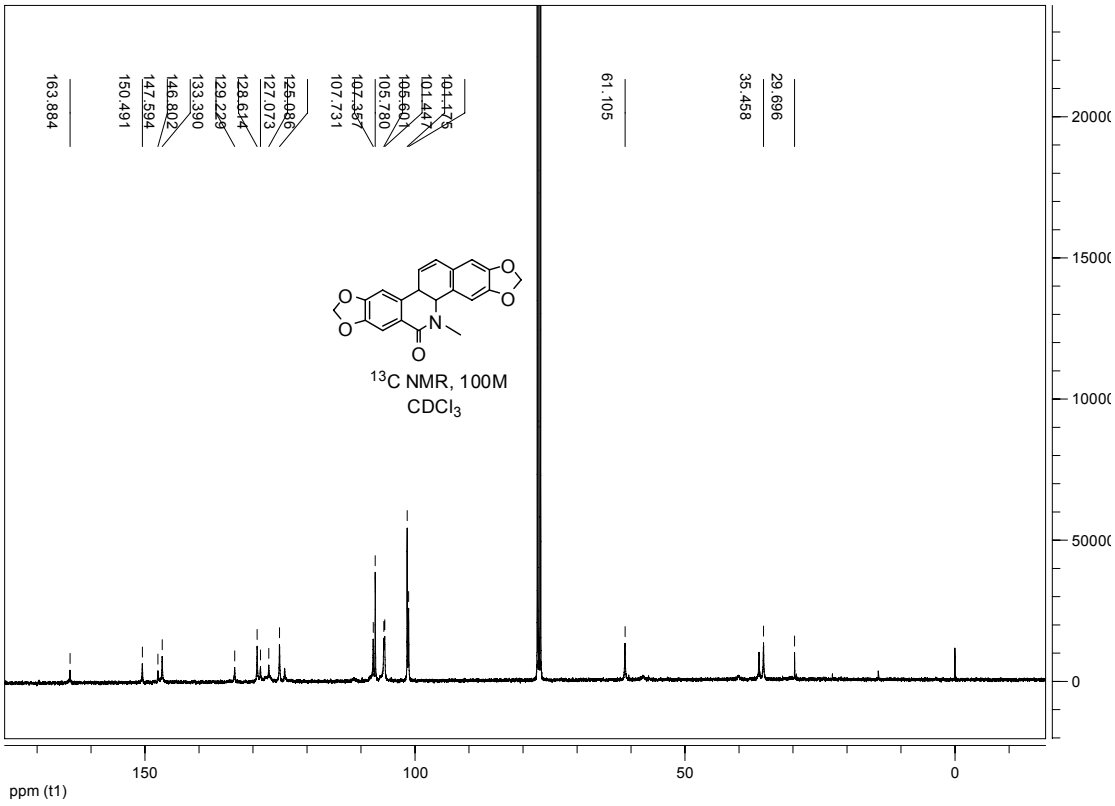

**17c**



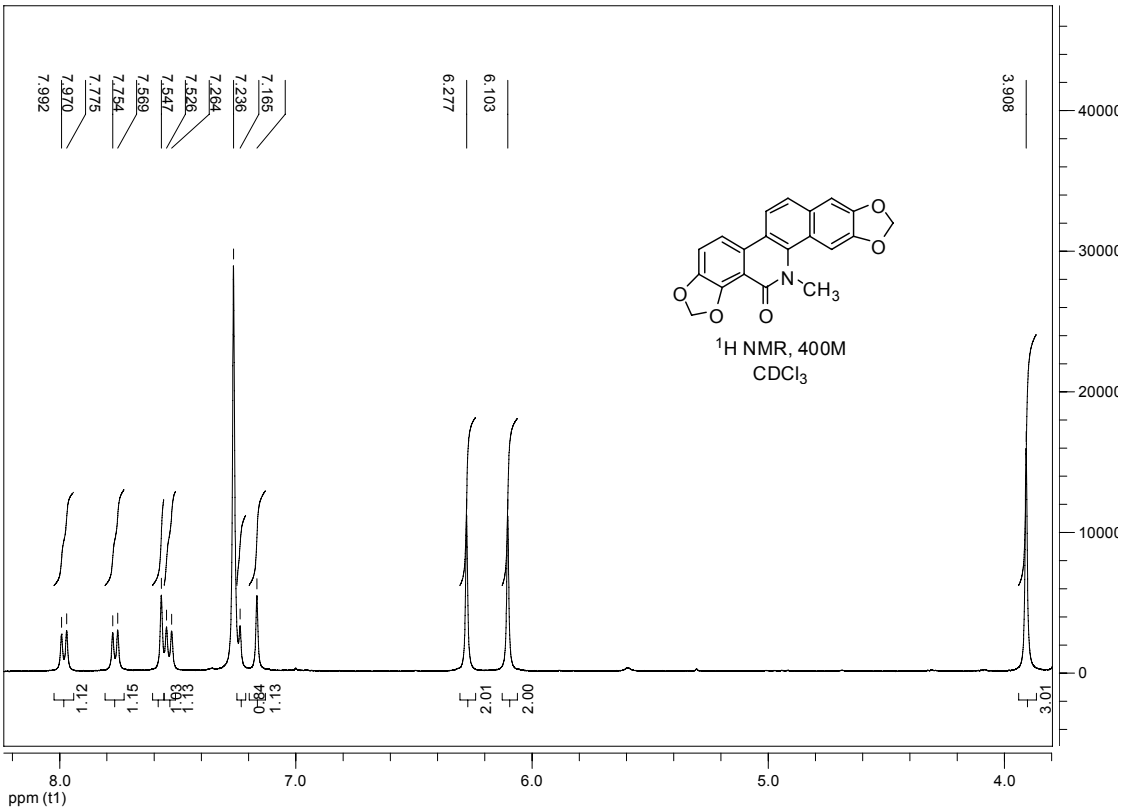




**17d**

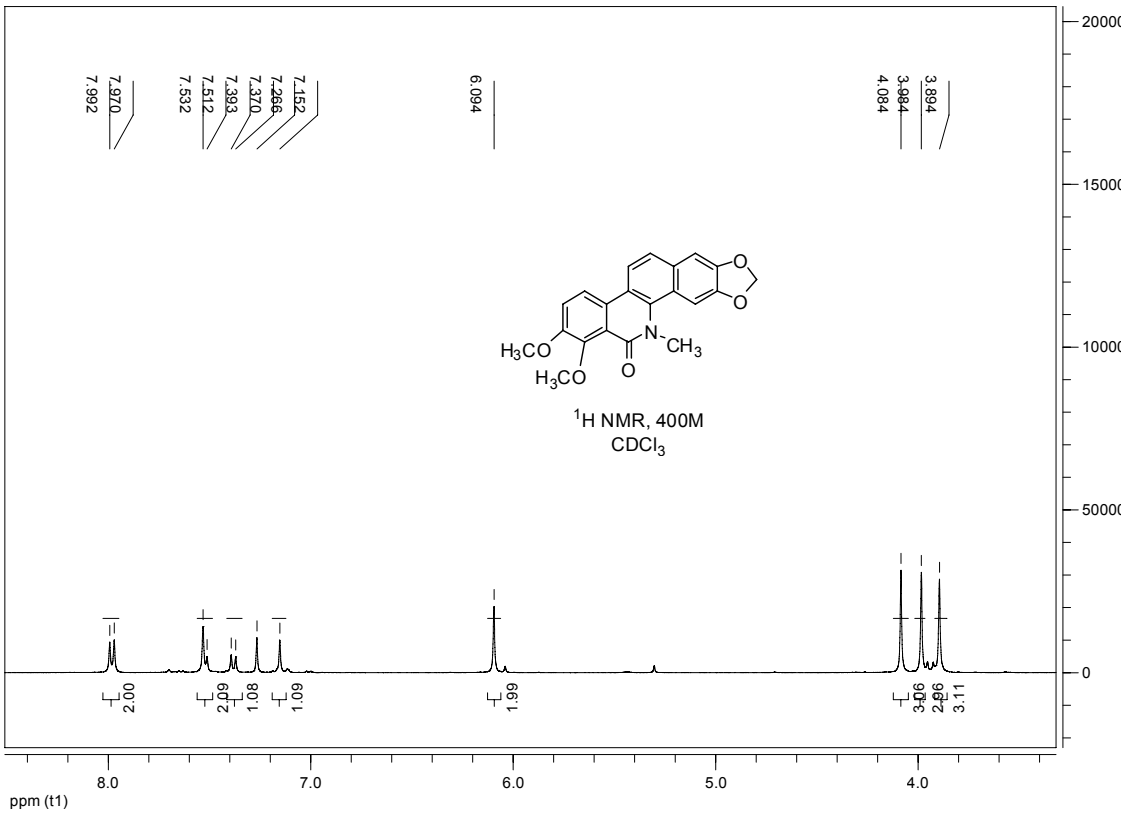


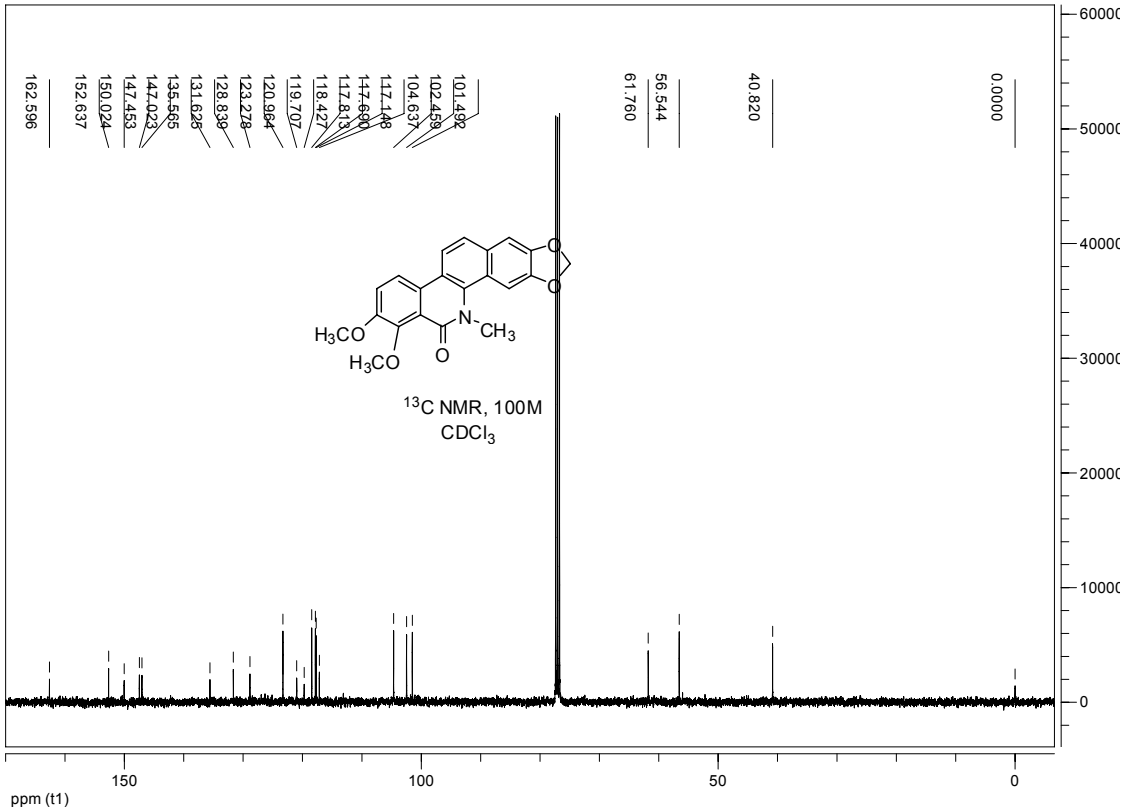




## Oxysanguinarine

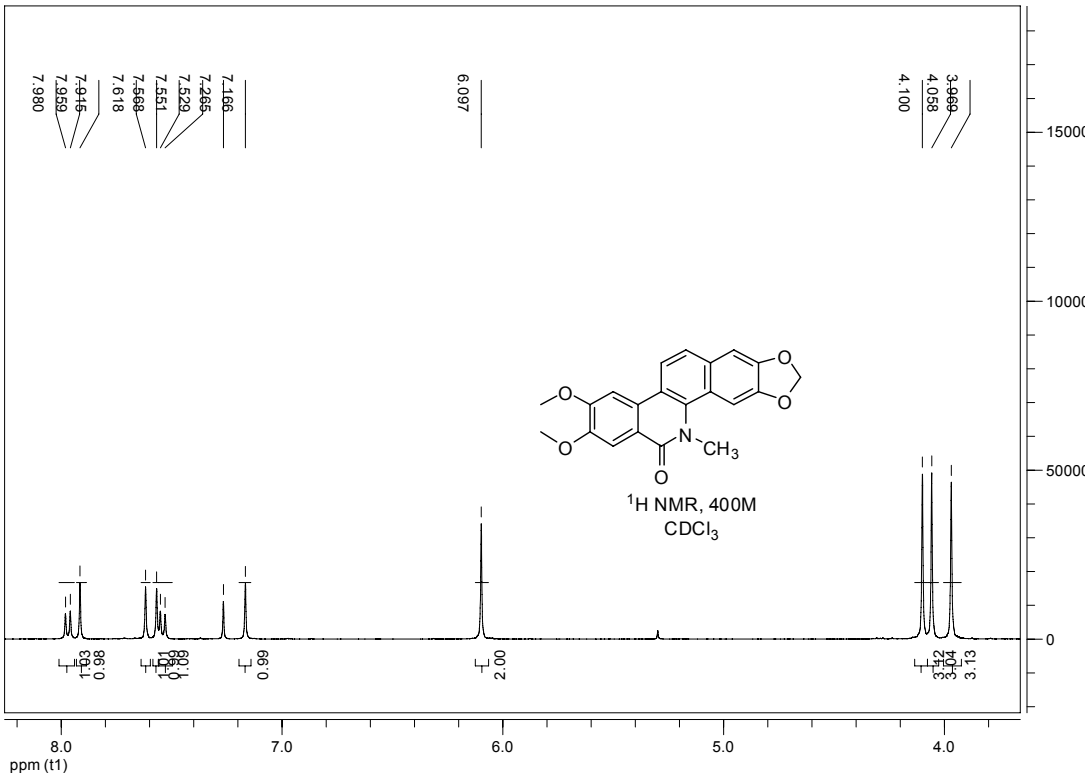


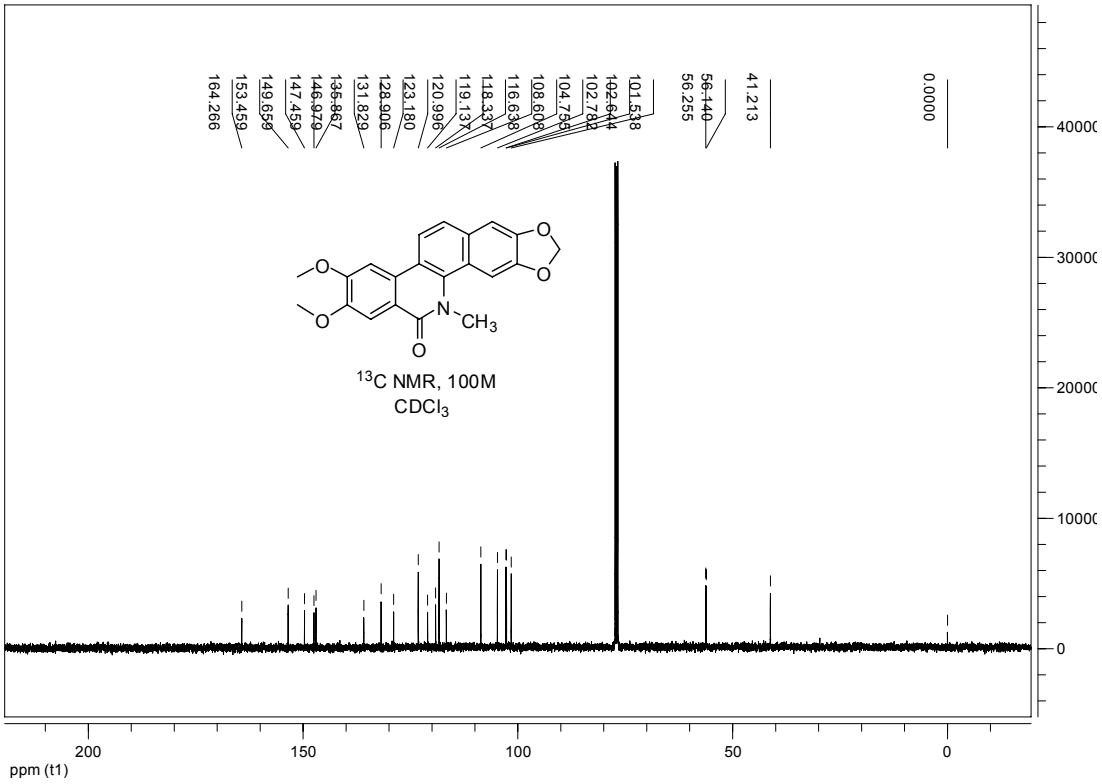

**Oxychelerythrine**



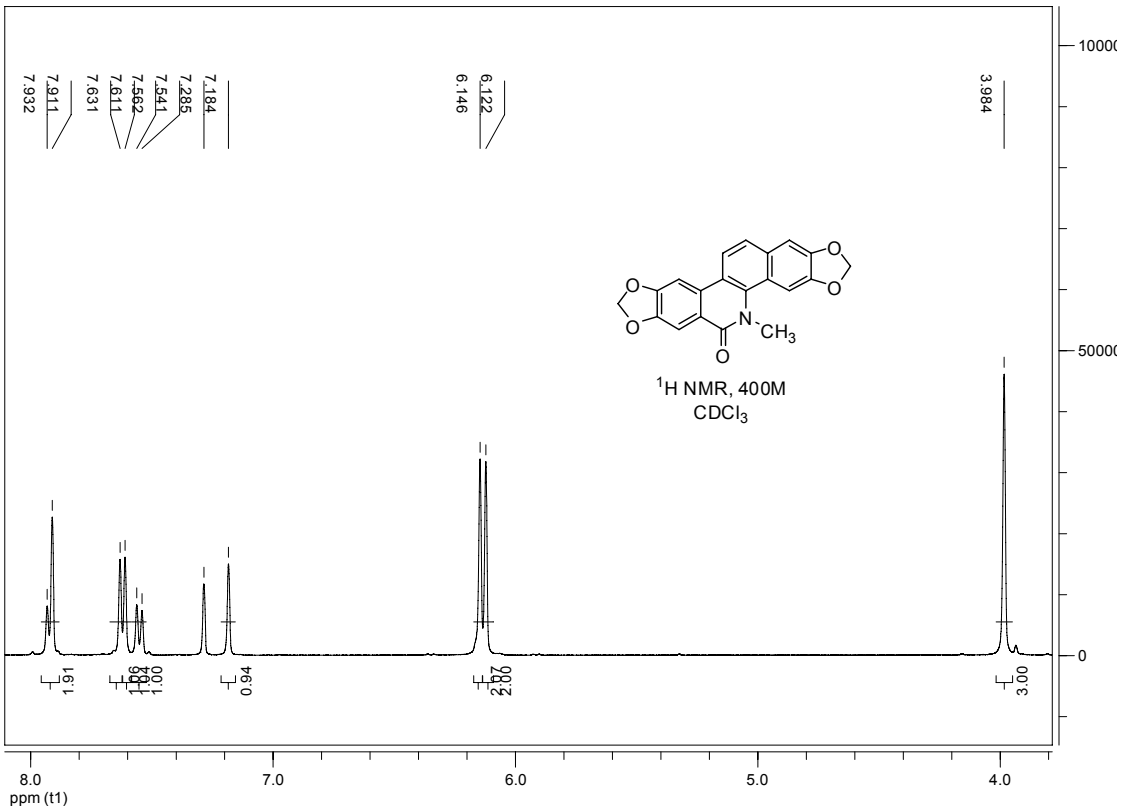



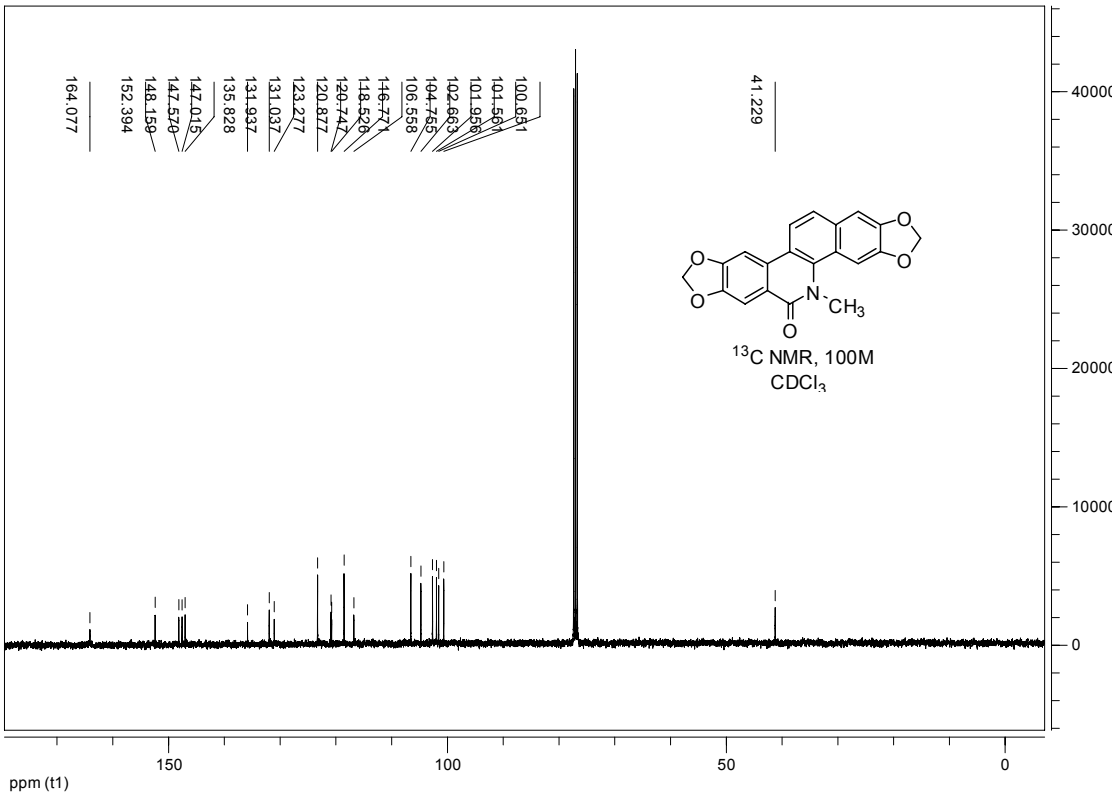

## Oxynitidine


7.980
7.959
7.915
7.618
7.568
7.551
7.529
7.265
7.166
6.097
4.100
4.058
3.969
1.93
0.98
1.00
0.96
2.00
3.12
3.04
3.13
$^1$H NMR, 400M
$CDCl_3$
ppm (t1)

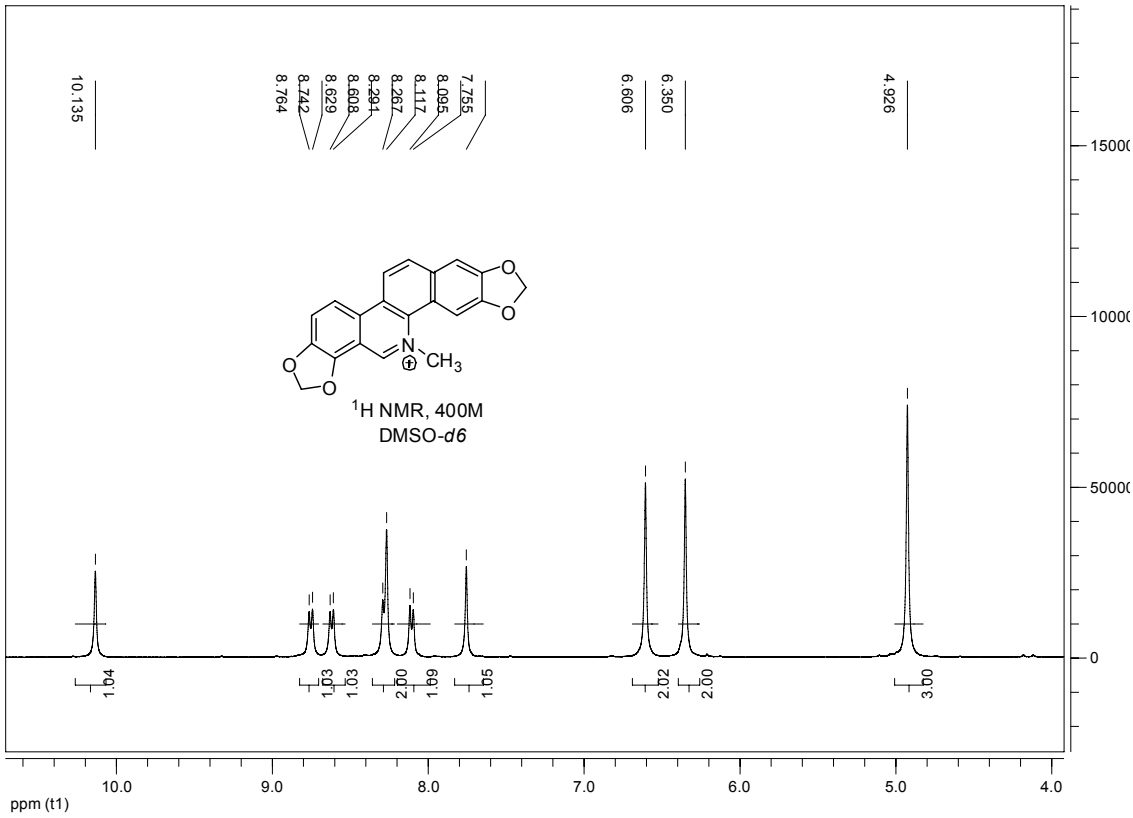

164.266
153.459
149.659
147.459
146.979
135.867
131.829
128.906
123.180
120.998
119.137
118.337
116.638
108.606
104.755
102.782
102.644
101.538
56.255
56.140
41.213
0.0000
$^{13}$C NMR, 100M
$CDCl_3$
ppm (t1)

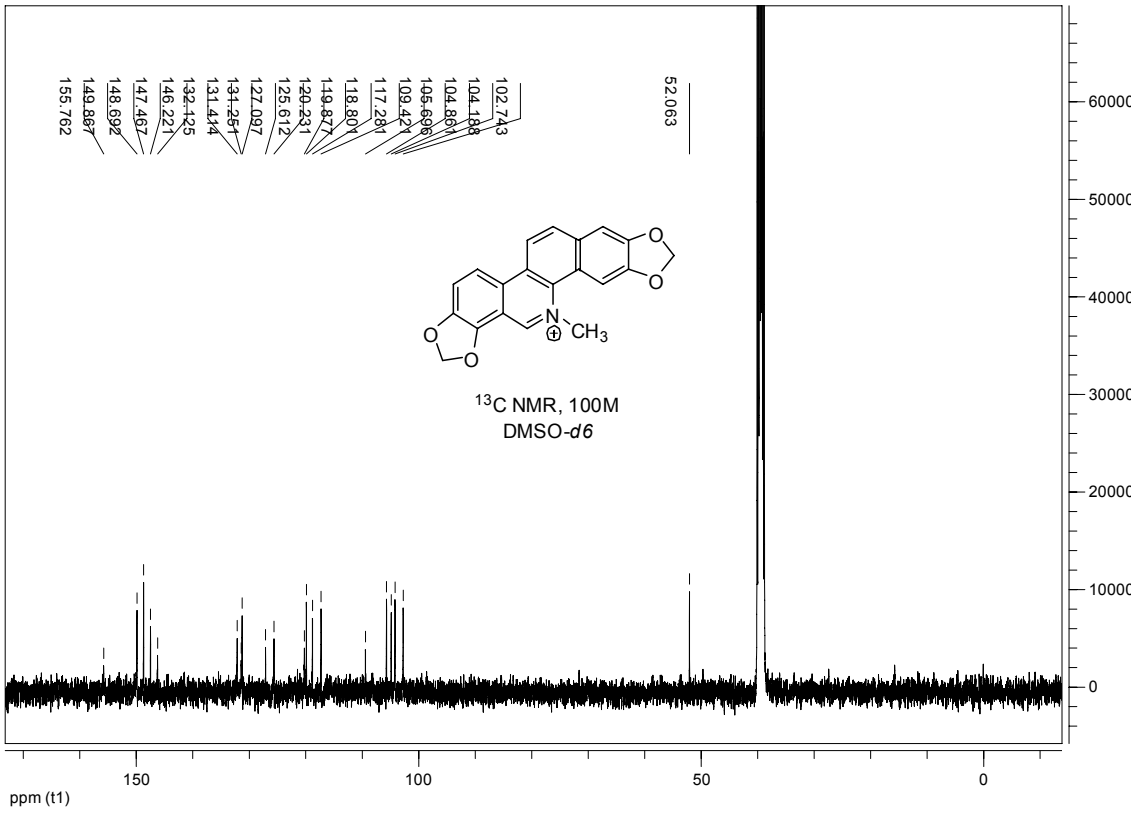
## Oxyavicine



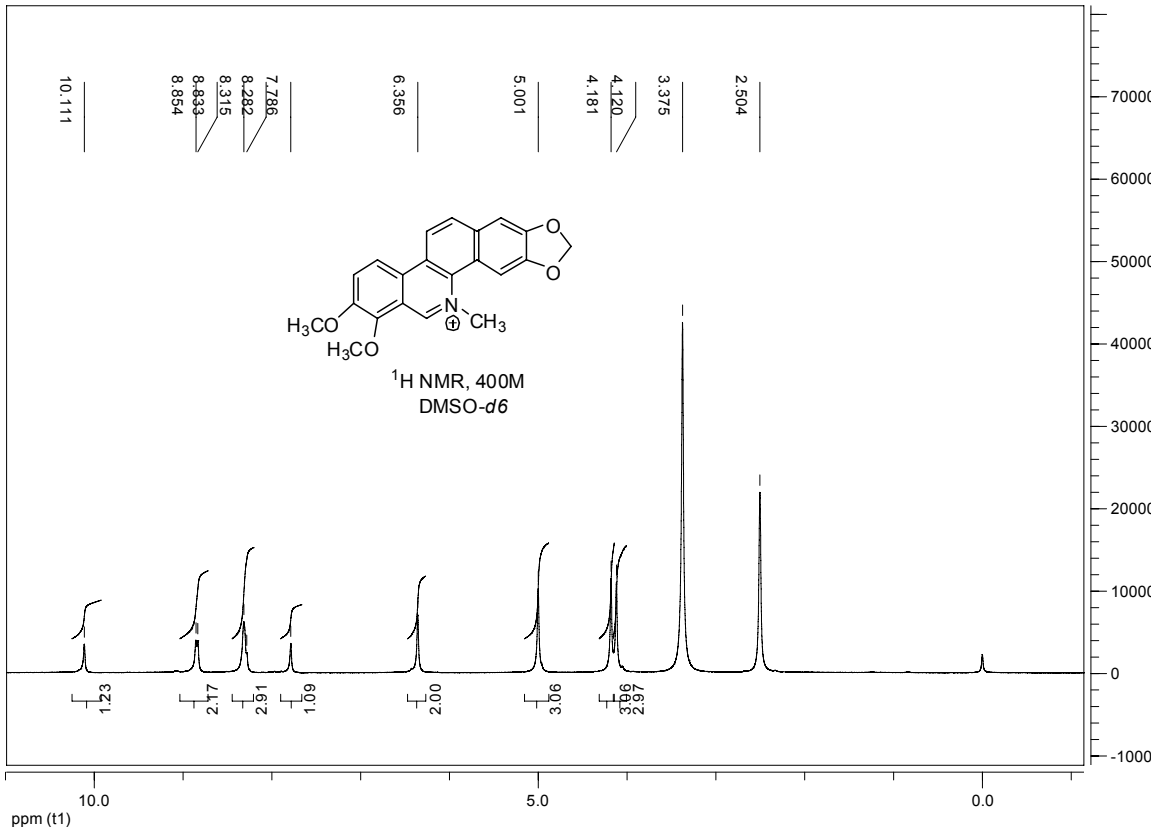



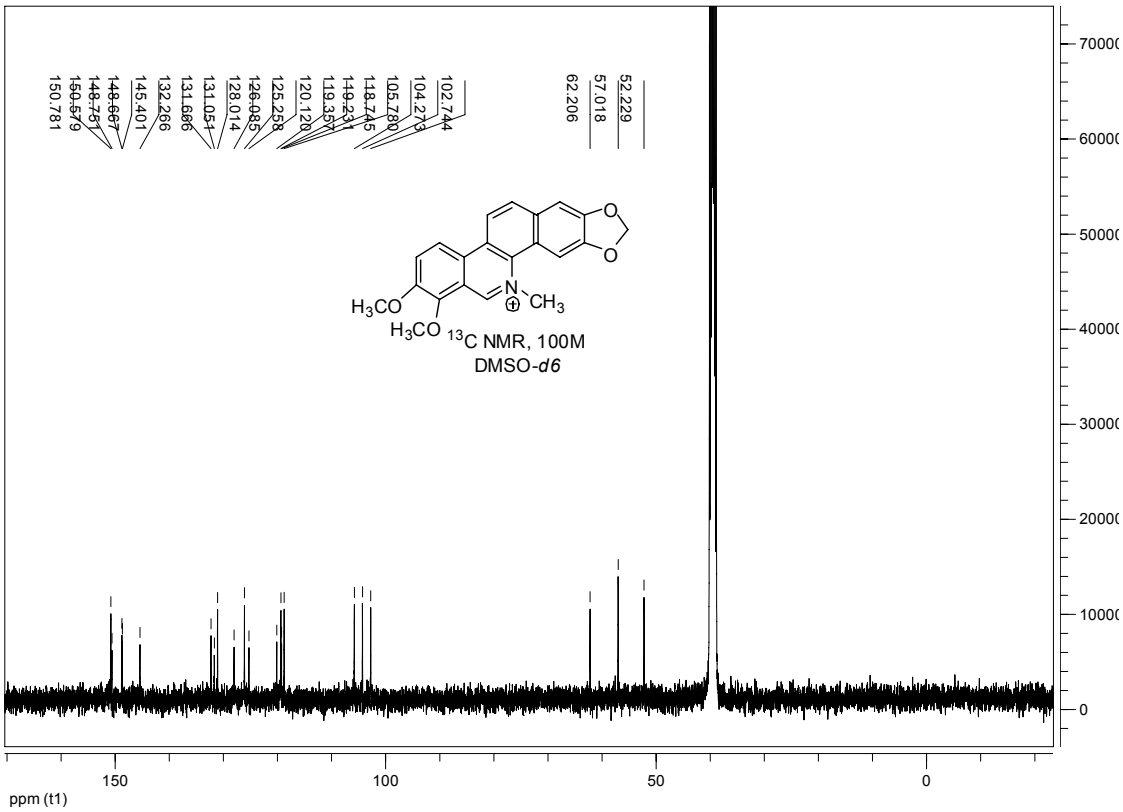

**Sanguinarine Chloride**



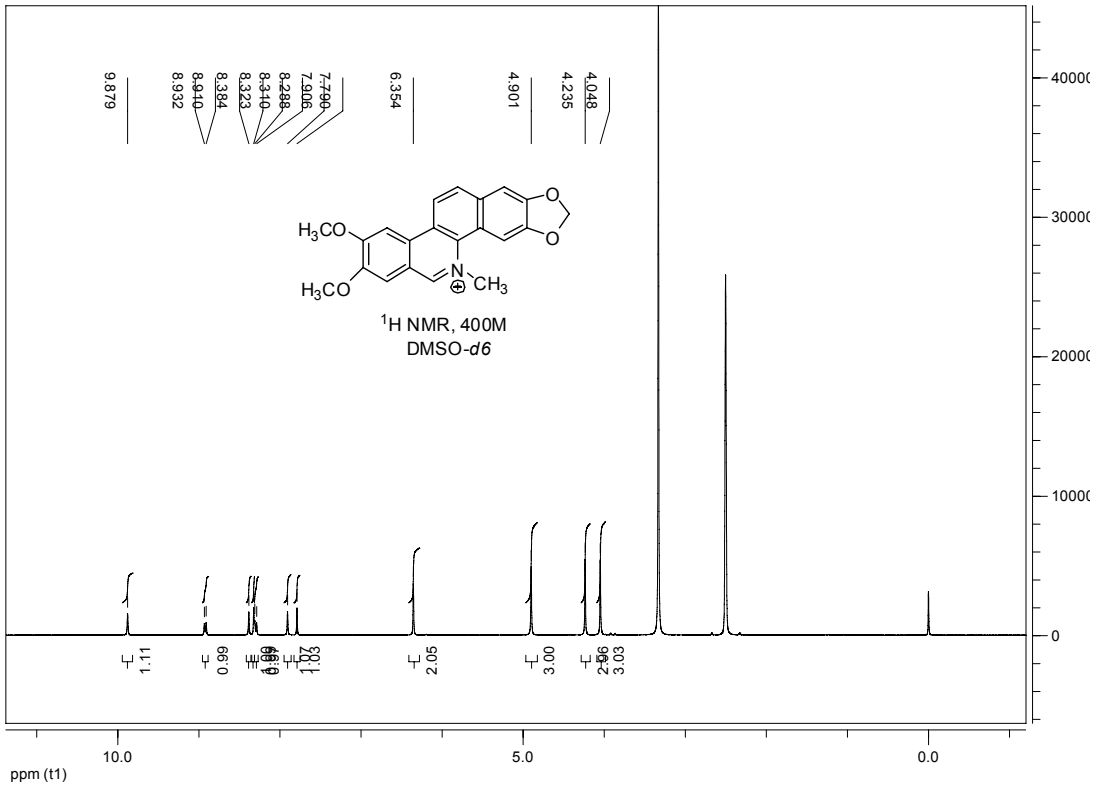



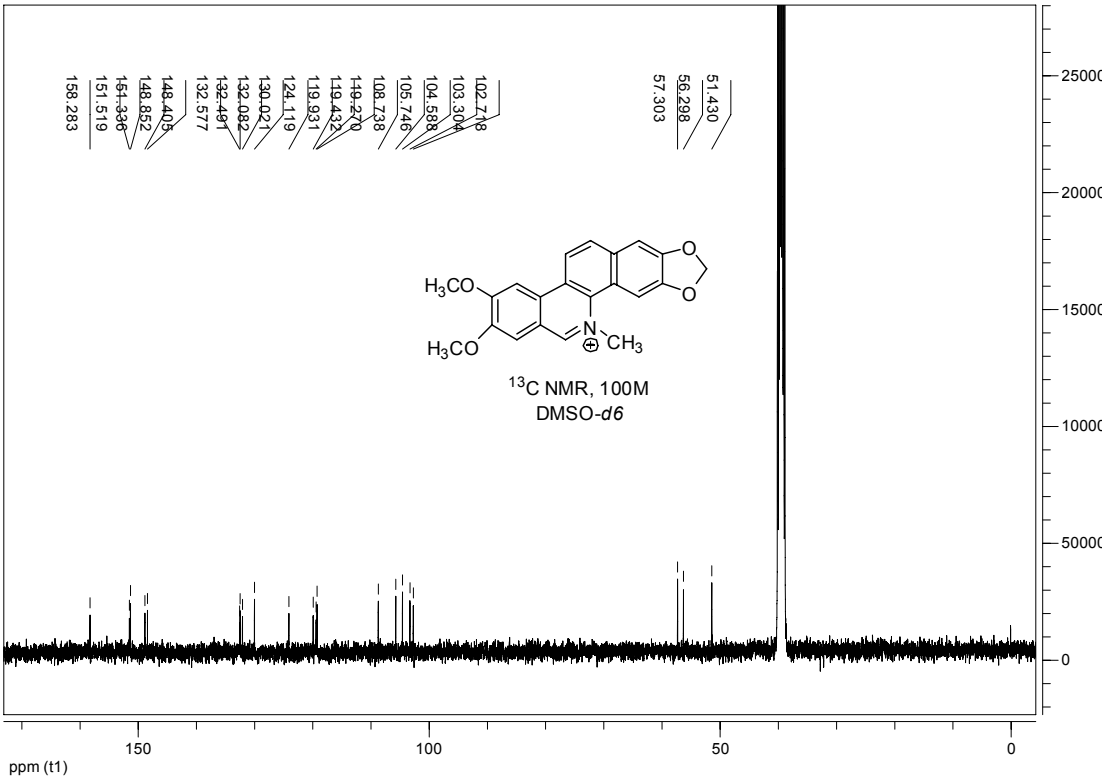

## Chelerythrine Chloride



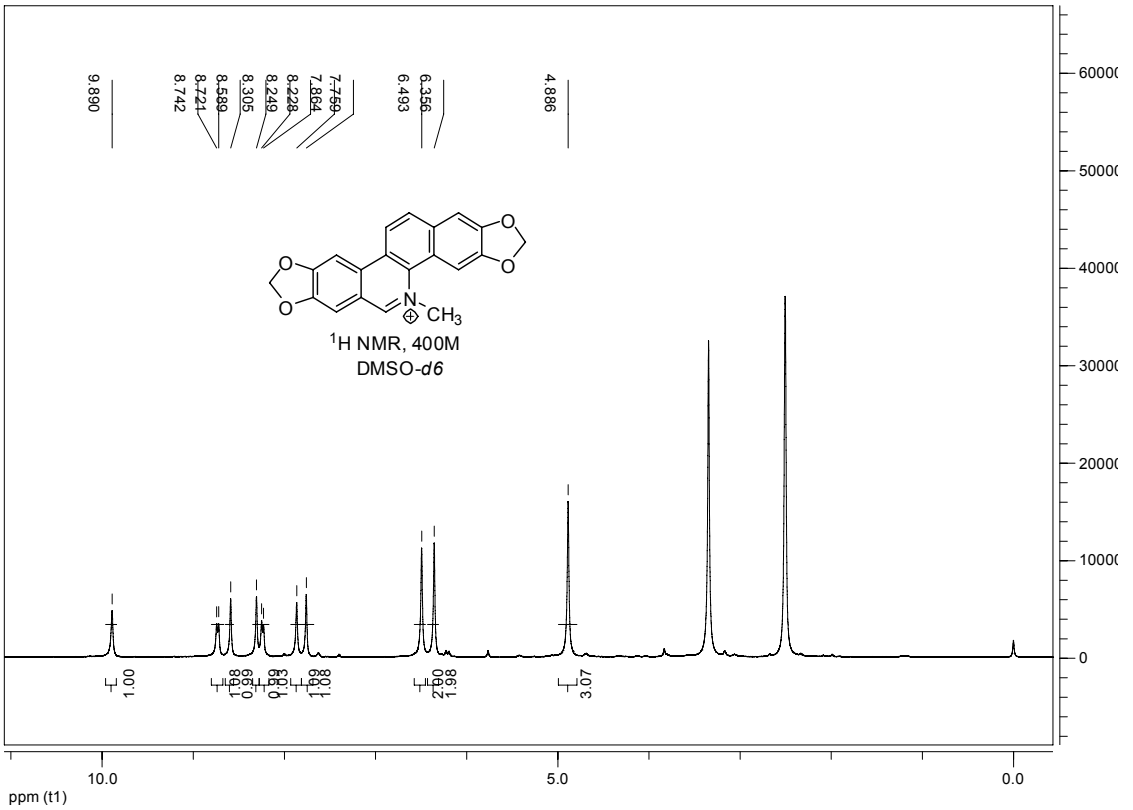



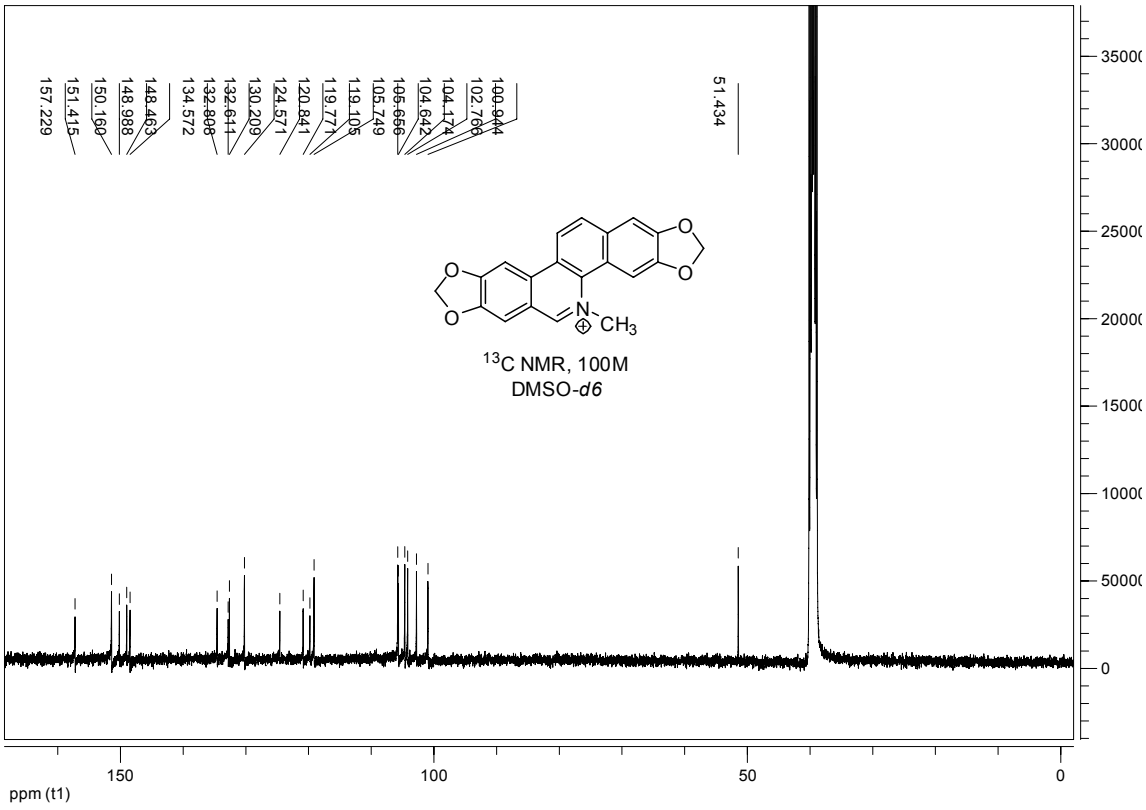

Ntidine Chloride




Avicine Chloride


9.890
8.742
8.721
8.589
8.305
8.249
8.228
7.864
7.769
6.493
6.356
4.886
1.00
0.98
0.98
0.99
1.08
1.00
2.00
1.98
3.07
$^1$H NMR, 400M
DMSO-*d6*
10.0
5.0
0.0
ppm (t1)


157.229
151.415
150.160
148.988
148.463
134.572
132.808
132.611
130.209
124.571
120.841
119.771
119.105
105.749
105.656
104.642
104.174
102.766
100.944
51.434
$^{13}$C NMR, 100M
DMSO-*d6*
150
100
50
0
ppm (t1)